





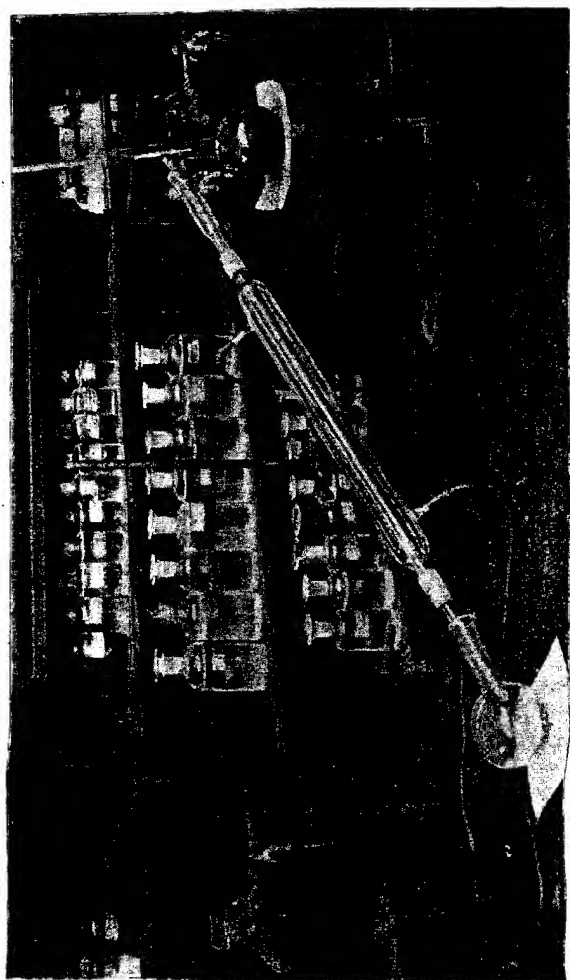








INTRODUCTION TO THE STUDY  
OF  
ORGANIC CHEMISTRY



# INTRODUCTION TO THE STUDY OF ORGANIC CHEMISTRY

A THEORETICAL AND PRACTICAL TEXT-BOOK  
FOR STUDENTS IN THE UNIVERSITIES  
AND TECHNICAL SCHOOLS

BY

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NEW AND ENLARGED EDITION

*With an Appendix containing Supplementary Practical Detail,  
forming with the text an Illustrative Laboratory Course*

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## PREFACE

THE favourable reception accorded to the first edition of this book is sufficient evidence of the soundness of its plan, and the thorough revision to which it has now been subjected has had for its aim rather improvement in detail than any fundamental alteration. Practically the whole work has been rewritten in the light of the author's experience of its use with large classes, and by relegating the less essential matter to a smaller type, it has been found possible both to simplify the book for beginners and those requiring a rapid review of the subject, and to increase its scope and usefulness. It need hardly be said that a reasonable knowledge of General Chemistry is assumed; the futility of commencing a specialised branch of a subject, before the foundations are secure, is (or should be) a truism.

The unsoundness of deductive treatment for beginners has now become axiomatic. It is easy for the student to commit generalisations to memory, and, reversing the natural order of growth, to fit the facts to them; but as an examiner the author knows how eminently unsatisfactory is the result. The average student thus instructed can, it is true, reproduce such general statements (which often, however, are not generalisations at all); but he learns to dislike what he inevitably comes to regard as the mechanical detail of experimental work, and breaks down when examined orally. The student of greater distinction feels on the other hand that the subject is finished, and loses that wholesome desire for personal experience which is the first condition of progress.

But the learner who proceeds experimentally, putting isolated facts together, forming generalisations from them, and using these generalisations to suggest further experiment, is following the natural method. Whatever his intellectual ability, he acquires, with reasonable industry, a singularly



vivid and intimate knowledge of his subject, and should he have the opportunity later to join the ranks of the pioneers, he will find that he has nothing to unlearn, and that original research, whether in pure or applied science, is but an extension of the methods with which he has become familiar.

After learning to know the properties of individual substances such as alcohol and aldehyde, the extension and consequent generalisation of this knowledge becomes in almost every case an intellectual necessity; and even where it is not so, it is surely better to acquire a certain power of observation, than the ability to repeat uncomprehended formulas.

As regards detail, the supplementary laboratory notes have been revised and extended, and will be found to embody an ample course of practical work. After due consideration it has been decided to retain them in their original position; minute details of quantity and manipulation belong to the laboratory, and not to the study, and reference to the end of the book has not proved to be inconvenient, but to afford a useful and easy exercise in collation. A short summary of operations and agents will be found at the end of these notes. The full synoptical charts have now been extended throughout the book; their utility as a means of expressing complex interrelations is too obvious to need comment.

The author takes this opportunity of thanking his correspondents for their kindly suggestions and criticisms, which he has borne in mind throughout the revision.

GUY'S HOSPITAL,  
LONDON BRIDGE,  
August, 1905.

ADDENDUM: December, 1910.—In re-printing another issue of the Second Edition opportunity has been taken to correct various slips and misprints, to which for the most part attention has been drawn by teachers and students using the book. The author takes this opportunity of thanking these correspondents for their courtesy and kindly interest.

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And numerous diagrams in the text.

If more were willing to regard the advancement of philosophy, than their own reputations, it were easy to make them sensible, that one of the most considerable services they could do the world, is to set themselves diligently to make experiments, and collect observations, without attempting to establish theories upon them, before they have taken notice of all the phenomena that are to be solved.—ROBERT BOYLE, *Sceptical Chymist*, Oxford, 1661.

## INTRODUCTORY.

**1. Organic and Inorganic Chemistry.**—Organic Chemistry is the Chemistry of Carbon Compounds. Up to the end of the eighteenth century there seemed a sharp line of demarcation between the transitory products formed in living organisms, and the relatively permanent mineral compounds. Not only were the organic products liable to change, but once changed they could not be formed again by artificial methods; all attempts to reconstruct them in the laboratory proved unavailing, and it seemed that the forms of matter associated with life were beyond the scope of ordinary chemical laws.

The successive discovery that these compounds contained carbon (Lavoisier, 1794), and were composed according to the same laws of definite and multiple proportions as those derived from minerals (Dalton, Berzelius, 1808–1818) rendered this view untenable; and when typical organic compounds such as urea (Wöhler, 1821) and acetic acid (Melsens, Kolbe, 1842–44) were made from inorganic materials, the apparent difference between the two great classes finally disappeared.

At the present time all organic compounds of simple constitution can be made artificially in the laboratory, and although many exceptions remain among the more complicated they are steadily diminishing in number, and will no doubt eventually conform to the general rule.

A separate classification is nevertheless convenient. The simpler organic compounds approximate to the common inorganic types, such as acids, bases and salts, but the majority of them are without counterpart, and being derived from a single element are related to one another in a peculiarly intricate manner. Their number and diversity moreover—upwards of 200,000 are known—render their inclusion in a textbook of general chemistry impracticable.



**2. Method of Study.**—Organic Chemistry is not a difficult subject when studied in the right way, but it requires patience and perseverance. The student is apt to be discouraged at first by his apparently slow progress; he may rest assured, however, that straightforward work in the laboratory will in due time bring its reward.

At the outset, the results seem disconnected, the theory somewhat intangible, and the facts difficult to retain. This is simply due to want of familiarity, and as laboratory experience is gained, and connections and analogies reveal themselves, the theoretical basis of the science gradually becomes concrete, and indispensable. Eventually, a moment arrives when some fresh observation or idea acts as a crystal to a refractory syrup, and the whole subject rapidly assumes a well-ordered, regular aspect.

It is only the first step which gives trouble; once the student has realized the wonderful logic of the science, his work ceases to be a labour. If he bears in mind the symbolic aspect of the subject while working at the bench, he will never lack material with which to clothe and vivify the symbols in the study; and it is such union of practice and theory which constitutes true knowledge.

The large number of names and formulae and apparent physical similarity of the simpler organic compounds, are confusing to the beginner, whose progress is therefore soon arrested unless he proceeds systematically on some very definite plan. Facility is most readily gained by the thorough study of a small selection of types, and, for this reason, we shall at once enter on the detailed consideration of representative substances, only venturing to generalise as we become familiar with the preparation, character and transformations of a sufficient number.

The names enclosed in parentheses throughout this book indicate the chemist who first prepared a substance, or obtained it in a state of purity; or who devised a process or apparatus, or explained a reaction. The dates are those of the years in which the account of the work was published. Since about 1875, abstracts of all chemical papers of importance have been published regularly in the *Journal of the Chemical Society*, on reference to which for the particular year (or in some cases, the following year), a short account of the work will usually be found, as well as a reference to the original paper. References to papers published before that date are given in *Watts' Dictionary of Chemistry* and *Beilstein's Handbuch der Organischen Chemie*. Students who wish to pursue chemistry seriously, should lose no opportunity of reading original papers, not only in English, but also in other languages, especially German and French.

PART I

Typical Compounds of Simple  
Constitution

SECTION I

THE ALCOHOLS AND ACIDS : ORGANIC RADICALS

CHAPTER I

PREPARATION OF PURE ALCOHOL

3. Alcohol or Spirit of Wine : Distillation.—Sweet liquids such as grape-juice cannot be kept unaltered in their natural state without special precautions, and under ordinary circumstances soon undergo a chemical change known as fermentation (§ 172). The liquid loses its sweetness and acquires intoxicating properties, and large quantities of carbon dioxide are generated during the whole course of the change. On boiling such a fermented product briskly in an open vessel it rapidly loses the newly acquired property, but the evolved vapour when cooled condenses to a liquid, which contains the active constituent in a more concentrated form. This condensed liquid, which is inflammable and considerably lighter than water, is known as *spirit of wine*. The active constituent of the spirit is called alcohol ; spirit of wine being simply alcohol somewhat diluted with water. Beer contains 4 or 5 per cent. of alcohol, and heavy wines as much as 20 per cent.

Spirit of wine\* was first prepared by some Arabian alchemists in the eleventh century, and the various "spirits" of commerce, which are more or less diluted modifications, suitably flavoured and coloured, are made at the present day by essentially the same process. The strong spirit used for chemical and manufacturing purposes, is generally made from sugar derived from potato starch (§ 172), and when rendered unfit

\* The matter in small type may be omitted on a first reading.

for human consumption by admixture with crude wood spirit (§ 43) and paraffin oil (§ 79), is allowed to pass free of duty under the name of denatured or *methylated spirit*.

The spirit stills used in factories are too bulky and complicated for laboratory purposes, and a much simpler distilling apparatus is employed in chemical investigations (see Frontispiece). The principle is the same, however, and is identical with that of the common retort and receiver. The liquid is boiled in a flask, which is provided with a side-tube for the exit of the vapour, so that a thermometer may be placed in the neck to indicate the boiling-point (Wurtz, 1855); and as liquid carbon compounds like alcohol are often volatile, the long sloping condenser tube which leads to the receiver is surrounded by a jacket, so that it may be cooled with water when necessary (Liebig, 1832).

The flask is usually heated by a small Bunsen flame, from direct contact with which it is protected by a piece of fine wire gauze, but in distilling volatile inflammable liquids it is safer to use a water-bath. A sand-bath or bath of melted paraffin wax is also occasionally employed. The bulb of the thermometer is covered with a thin layer of fibrous material such as cotton-wool, so that it may not be superheated by hot gases from the flame; when possible it is lowered until the whole of the mercury column is immersed in the vapour, but it must not project into the bulb of the flask. To secure uniform boiling two or three fragments of dry, porous earthenware are placed in the liquid.

The distillation serves in this case the double purpose of purification and identification. In the first place the volatile alcohol is obtained entirely free from dissolved solids and colouring matter; and in the second place the presence of a volatile constituent and concurrent distillation of water, are indicated by the steady rise of the boiling-point until it reaches 100°. Distillation is always used for one or other of these purposes.

**4. Purification of Alcohol: Fractional Distillation or Rectification.**—The separation of the water is a more complicated process. As the boiling-point rises steadily during the distillation, it is obvious that the distillate is a mixture, and this conclusion is confirmed by collecting it in separate portions or fractions. The early fractions not only boil at a lower temperature than the later ones, but their specific gravity is lower, and gradually

increases as the distillation progresses, until the last fraction is nearly as dense as water. It is evidently possible by redistilling these fractions to effect a further separation of the two liquids, and such a systematic distillation is known as fractional distillation or rectification.

The mixture in the first place is steadily distilled almost to dryness, the successive fractions being collected in separate receivers according to their boiling points.

*First fractionation of a mixture of 50 c.c. of alcohol and 50 c.c. of water.*

Fraction . .	x-82° (head)	82-87°	87-92°	92-97°	97-x° (tail)
Volume . .	20 c.c.	16 c.c.	13 c.c.	21 c.c.	29 c.c.

The fractions are then redistilled, but owing to their altered composition no longer pass entirely over at the original temperatures. The composition of the vapour from the boiling liquid is governed by the condition that its total vapour-pressure is equal to that of the atmosphere; hence, as at any particular temperature the vapour-pressure of the alcohol is greater than that of the less volatile water, the proportion of alcohol in the vapour is greater than in the boiling liquid. The weaker the liquid is in alcohol, the greater the disparity. Alcohol thus distils the faster from the stronger fractions, and water from the weaker, so that the result of the second fractionation is to increase the bulk of the end fractions at the expense of the intermediate ones.

*Second fractionation.*

Fraction . .	x-82° (head)	82-87°	87-92°	92-97°	97-x° (tail)
Volume . .	32 c.c.	5 c.c.	11 c.c.	14 c.c.	36 c.c.

The separation is rapidly increased by each subsequent fractionation, and by the end of the third the greater part of the alcohol and water have already passed into the head and tail fractions, the boiling points and specific gravities of which now approximate to those of the pure liquids.

*Third fractionation.*

Fraction . .	x-82° (head)	82-87°	87-92°	92-97°	97-x° (tail)
Volume . .	44 c.c.	0 c.c.	1 c.c.	11 c.c.	42 c.c.
Sp. gr. . .	0.856	—	—	—	0.991
Sp. gr. of original constituents .	0.835	—	—	—	1.000

The somewhat tedious process of fractionation is greatly accelerated by partially cooling the vapours before they enter the condenser, so that the less volatile portions are continuously returned to the flask; and a nearly complete separation may thus often be effected in a single distillation. For this purpose a round-bottomed flask is fitted with a long wide tube or still-head, the upper part of which is provided with a side-tube and

thermometer, as in the ordinary distilling-flask; with a plain tube, however, the vapour tends to pass up the middle, without coming into contact with the condensed liquid running down the sides, and various fractionating columns have been designed in order to remedy this defect.

Hempel's column (1881) is filled with large glass beads which break up the stream of vapour, and bring it into contact with a large surface of condensed liquid. Young's pear column (1902), which is the most convenient for ordinary purposes, consists of a vertical series of pear-shaped bulbs, five to twelve in number (Fig. 1). These bulbs are shaped so that they set up eddies in the vapour, and prevent the formation of a central stream; at the same time they largely increase the area of the condensing surface. The vapour is thoroughly washed by the drops of condensed liquid which fall steadily from bulb to bulb. Probably the most efficient column at present available is Young's evaporator still-head (1902).



Fig. 1. Young's Pear Still head.

The strongest alcohol obtainable on a commercial scale by ordinary distillation is known as *rectified spirit*, and has a specific gravity of 0.835 at 15°; it contains about 15 per cent. of water. *Proof spirit* is defined legally as spirit having a specific gravity of 0.923 at 51° F., and contains only 49 per cent. of alcohol. *Methylated spirit*, which consists of rectified spirit, mixed with wood spirit and paraffin oil, can be obtained under licence for chemical purposes free from paraffin; after boiling with caustic soda to eliminate acetone and other impurities, and redistilling, it may be employed for most chemical operations instead of the more expensive pure alcohol. Rectified spirit may now, however, (1905) be obtained free of duty for scientific use in approved institutions. Alcohol is employed in large quantities in the manufacture of dyes and drugs, and next to water is the solvent most frequently used in chemistry.

5. Purification of Alcohol: Absolute Alcohol.—By slowly distilling rectified spirit through a very efficient still-head. a

fraction may be separated having a specific gravity of about 0.810 at 15°, and this is the strongest obtainable by distillation; it contains about 5 per cent. of water. If, however, rectified spirit be digested with an appropriate desiccating agent, such as potassium carbonate or quicklime, and then redistilled, a spirit is obtained which has a still lower gravity, and therefore contains less water (Lully, thirteenth century). By repeating this treatment, a liquid is ultimately obtained, whose boiling-point and specific gravity are constant, and cannot be further

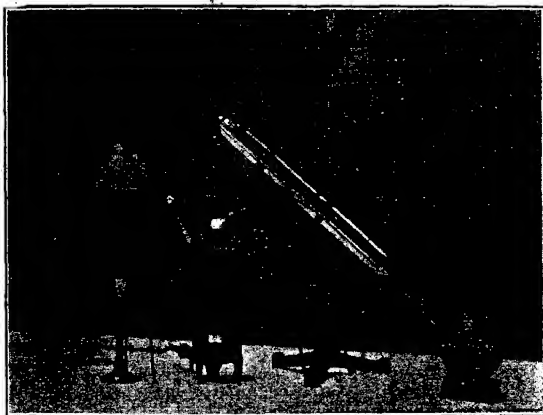


Fig. 2.—Dehydration of Rectified Spirit.

The spirit is boiling with quicklime in the flask with the inverted condenser, and the dehydrated product from a similar operation is being separated from the slaked lime by distillation.

reduced. This product is therefore pure, and is termed *absolute alcohol*.\*

*Absolute alcohol* is prepared in the laboratory by boiling rectified spirit for an hour or two with half its weight of fresh quicklime in lumps (Souberain, 1839). The operation is carried out in a large flask, which is heated on a water-bath, and connected with an inverted condenser (Fig. 2) to prevent the escape of the vapour. When the lime has slaked and swollen to a semi-solid paste, the condenser is arranged for ordinary

\* The word *alcohol* is probably a corrupted contraction of (*spiritus alcalisatus*, i.e. spirit which has been treated with alkali (Kopp).

distillation; the vapour is led into it through a bent tube, and the heating on the water-bath continued until liquid ceases to pass over. A flame must not be used, nor should the alcohol be filtered from the lime before it is distilled.

If the original spirit contains more than 8 or 9 per cent. of water, the distillate must be treated again with half the quantity of quicklime; but it is difficult to eliminate the last traces of water. Absolute alcohol is also made by slowly filtering spirit through quicklime, the process extending over ten days or more (Squibb, 1887); thus prepared, however, it is liable to contain traces of ether. The "absolute alcohol" of commerce usually contains about 2 per cent. of water.

*Alcohol*,  $\text{CH}_3\text{CH}_2\text{OH}$ \* (Lowitz, 1796) is a colourless liquid, which has a pleasant odour and hot taste, and burns with a non-luminous flame. It boils at  $78.3^\circ$  under normal pressure,† and at  $-112^\circ$  freezes to a white crystalline solid; its specific gravity is 0.794 at  $15^\circ$ . Pure alcohol is hygroscopic.

When spirit contains 4 or 5 per cent. of water, it boils at a slightly lower temperature ( $78.15^\circ$ ) than anhydrous alcohol, and hence cannot be further concentrated by further distillation, unless a third liquid—such as benzene—is added, which will form with the water and alcohol a mixture of still lower boiling-point (Young, 1902).

**6. Criteria of Purity.**—A substance is pure and a chemical individual when its physical properties are constant and these physical tests are the ultimate criteria of purity.

Mixtures such as 95 per cent. alcohol may also have constant boiling-points, but are distinguished from pure substances by the variation in their composition when they are redistilled under a different pressure.

It is usually convenient to prove the presence or absence of specific impurities by chemical tests. White anhydrous copper sulphate is slowly converted into the blue hydrated salt when added to alcohol containing water. The yellow solution of barium oxide in alcohol is rendered milky when moist alcohol is added, owing to the precipitation of the insoluble hydroxide. Paraffin oil, in which alcohol is soluble, but water insoluble, is rendered turbid by the presence of water in the spirit.

**7. Synopsis.**—Alcohol, prepared by the fermentation of sugar, is separated from dissolved solids by simple distillation, and from water by fractional distillation. The last portions of water are usually removed by chemical means. The alcohol is known to be pure and a chemical individual by the constancy of its physical properties.

\* Formulae such as these are inserted for convenience; they are explained in Chapter xii.

† For correction of boiling points, see Laboratory Notes.

## CHAPTER II

### ANALYSIS OF ALCOHOL AND DETERMINATION OF ITS FORMULA

**8. General Actions of Alcohol : Necessity of Analysis.**—When a product has been purified, and its individuality has been established by the constancy of its physical properties its examination from a chemical standpoint becomes possible. As in all scientific work, the method is that of experiment, guided by analogy. Sometimes the nature of a substance is obvious from the method of its formation, as in the preparation of the salt of an organic acid ; and in such cases only confirmatory evidence of identity is needed. At other times, when there is no such guide, analogies must be sought for.

Although alcohol is combustible, and very different physiologically, it resembles water and the metallic hydroxides in many of its chemical relations. Many salts are dissolved by it, and the crystals which separate from such solutions often contain loosely combined alcohol, analogous to water of crystallisation. *Calcium chloride alcoholate*,  $\text{CaCl}_2 \cdot 3\text{C}_2\text{H}_5\text{O}$ , is a definite crystalline compound, which like the hydrate is decomposed by heat. The action of sodium on alcohol is similar to its action on water, hydrogen being evolved and a sodium derivative formed. Alcohol slowly and partially neutralises acids, and in this resembles the mineral alkalies to a certain extent.

But although its general character is fairly clear, the chemical nature of alcohol cannot be exactly defined without quantitative examination. The physical differences between organic compounds are much less marked than in parallel inorganic cases, and it is necessary to analyse them and determine their formulæ before further progress can be made. It is largely for this reason that the systematic study of Organic Chemistry, although the oldest branch of the science, was followed without much success until quantitative methods, and the consequent theories, were developed.

**9. Detection and Estimation of Carbon and Hydrogen.**—That alcohol contains carbon and hydrogen is proved by its con-



version into carbon dioxide and water when fully oxidised (Lavoisier, 1794). The spirit is conveniently burned in a crucible beneath an inverted funnel, from the stem of which the gaseous products are aspirated. These are drawn through a cooled, empty vessel, and then through a flask of lime-water; water condenses in the first, and calcium carbonate is precipitated in the second. With the exception of oxygen, the presence of which must usually be established by quantitative analysis, no other element can be detected.

The proportion of carbon and hydrogen is determined by burning the substance in a slow current of air or oxygen in presence of copper oxide, the combustion being effected in a hard-glass tube about three feet long, which is heated in a gas furnace (Fig. 3).

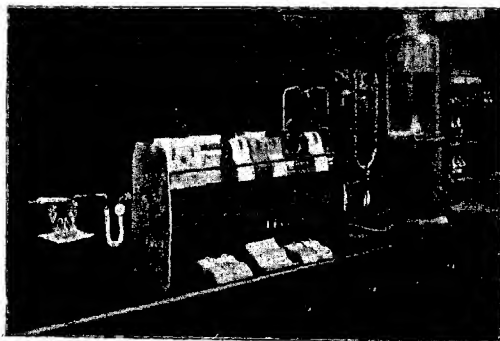


Fig. 3.—Estimation of Carbon and Hydrogen by Combustion with Copper Oxide.

The water from the large jar passes through a T-piece into one or other of the smaller jars behind the furnace, containing respectively air and oxygen. The gases thus expelled pass through a T-piece into the drying apparatus. The large tubes are filled with pumice soaked respectively in strong potash solution and concentrated sulphuric acid, which are forced up through T-tubes from the conical reservoir flasks for a few minutes before each combustion. The small bottles at the top contain dilute air passes into the combustion tube, in which the substance and main portion of the copper oxide are situated at the parts from which the clay furnace-tiles have been removed. The burnt gases leaving the tube pass through a U-tube containing sulphuric acid and pumice (most of the water condensing in the small bulb), and then through the three-bulb vessel containing strong potash. The small horizontal tube above the bulbs contains more pumice and sulphuric acid, to retain the moisture given off by the potash solution.

The granulated oxide, which is placed in the middle and further end of the tube between plugs of asbestos, is first heated to redness in a current of purified air, to remove all traces of moisture and organic matter. A known weight of the substance, in a small glass bulb, or in the case of solids in a narrow platinum boat, is then introduced into the end next the air inlet, and gradually heated to redness. Most of the substance is

burned in the air, whilst the oxidation of any that is volatilised unconsumed is completed by the red-hot copper oxide.

When the oxidation is finished, the current of air is continued until the residual carbon dioxide and steam have been swept into the absorption bulbs; the reduced copper is thus also re-oxidised, so that the tube is ready for a fresh combustion when the part containing the boat has cooled.

The carbon dioxide and water vapour are carried with the excess of air through a series of two vessels, which contain calcium chloride and potash or equivalent absorbent substances. The water is absorbed by the calcium chloride, and the carbon dioxide by the potash, so that the weight of the oxidation products is given by the increase in weight of these vessels (Liebig). The operation lasts about two hours.

In some careful combustions of alcohol the following results were obtained—

- I. 0.2063 gram gave 0.3931 gram  $\text{CO}_2$  and 0.2475 gram  $\text{H}_2\text{O}$ .
- II. 0.2856 gram „ 0.5427 gram  $\text{CO}_2$  and 0.3365 gram  $\text{H}_2\text{O}$ .
- III. 0.1989 gram „ 0.3796 gram  $\text{CO}_2$  and 0.2351 gram  $\text{H}_2\text{O}$ .

**10. Calculation of Percentage Composition.**—As the percentage composition of carbon dioxide and water is known, the data required for the calculation of the percentage composition of alcohol are complete. In the first combustion the weight of the carbon in the portion taken is

$$0.3931 \times \frac{3}{11}^* = 0.1072 \text{ gram};$$

its percentage is therefore

$$C = 51.96.†$$

The weight of hydrogen is similarly

$$\frac{0.2475}{9}^* = 0.0275 \text{ gram};$$

its percentage is therefore

$$H = 13.33.$$

The oxygen is determined by difference, as there is no satisfactory method for its estimation; in this case its percentage as there is no other element present, is

$$O = 100.00 - (51.96 + 13.33) = 34.71.$$

The duplicate analyses give results which agree with these within the limits of experimental error (§ 11), and the composition of alcohol, like that of all pure substances, is therefore constant. It was first ascertained by exploding the vapour with oxygen (De Saussure, 1808).

**11. Calculation of Empirical Formula.**—All matter must be considered from a chemical point of view as composed of atoms

---


$$^* \frac{C}{\text{CO}_2} = \frac{12}{44} = \frac{3}{11}; \quad \frac{H_2}{\text{H}_2\text{O}} = \frac{2}{18} = \frac{1}{9} \quad \dagger \frac{0.1072}{0.2063} \times 100.$$

of definite weight. The relative numbers of the atoms are proportional to the quotients of the percentages by the respective atomic weights (Dalton, 1808). The ratio in the case of alcohol is

$$N_o : N_h : N_c = \frac{51.96}{12} : \frac{13.33}{1} : \frac{34.71}{16} :$$

this on simplification becomes

$$N_o : N_h : N_c = 4.33 : 13.33 : 2.17.$$

so that the oxygen atoms are the fewest. But fractions of atoms are inadmissible, and dividing throughout by the smallest number, the numbers become

$$N_o : N_h : N_c = 1.99 : 6.15 : 1.$$

Here again fractions are obtained. If, however, it be assumed that the small differences from whole numbers which now remain are due to experimental error, the numbers fall into the simple ratio

$$N_o : N_h : N_c = 2 : 6 : 1,$$

making the formula



Empirical Formula of Alcohol.

The validity of this assumption is proved by the agreement, within the limits of experimental error, of the percentages calculated from this formula with those worked out from the three analyses. A formula is always checked in this way, apart from theoretical considerations.

Analysis of Pure Alcohol.

	Found.			Calculated for $C_2H_6O$ .
	I.	II.	III.	
Carbon	51.96	51.83	52.05	52.17
Hydrogen	13.33	13.09	13.13	13.04
Oxygen	34.71	35.08	34.82	34.79
	100.00	100.00	100.00	100.00

A formula showing merely the composition of the substance, and the ratio in which its atoms are combined, is termed an empirical formula (Dalton). An empirical formula affords no information as to the size of the chemical units or molecules, and until this is known there is no evidence whether the formula of the reacting unit is identical with, or some multiple of it. The molecular weight is therefore also determined.

**12. Determination of Vapour Density and Molecular Weight.**—The molecular weight of a volatile liquid is deduced from the ratio of the weight of its vapour to that of the same volume of hydrogen at the same temperature and pressure. These volumes contain the same number of molecules (Avogadro,

1811), and the weights of the individual molecules are therefore in the same ratio as the weights of the vapours. In practice it is inconvenient to compare the vapour directly with hydrogen, and air is used, the density being calculated from the known specific gravity of the lighter gas.

In Victor Meyer's method (1878) the air displaced from an appropriate vessel by the vapour of a known weight of the liquid is collected and measured, and its weight calculated. The displacement vessel (Fig. 4) consists of a long vertical tube having a cylindrical bulb at the lower end, and near the upper end a side tube leading to a small pneumatic trough. The bulb and part of the tube are heated by steam or other saturated vapour at a constant temperature, well above the boiling-point of the substance, the steam, etc., being generated in a cylindrical glass jacket surrounding the displacement tube.

When the air ceases to expand, and has therefore attained the temperature of the jacket, a weighed quantity of the liquid, enclosed in a miniature stoppered tube, is dropped into the bulb, the stopper of the displacement vessel being quickly replaced. The liquid slowly volatilises, but the vapour being heavier than air remains at the bottom, and an equal volume of air at the same temperature and pressure is expelled into the graduated vessel at the trough. Here the air is measured, and its temperature and pressure are noted; it contracts on passing into the cold measuring tube, but this is immaterial, as it is the weight which is required.

In a particular experiment the vapour of

0.0623 gram of alcohol

displaced

34.0 c.c. of air,

measured over water at 20° and 752 mm. The weight of this volume of air is

0.0396 gram,\*

and the specific gravity of the vapour is therefore

$\frac{0.0623}{0.0396}$  or 1.57

Its vapour density, or specific gravity, referred to hydrogen is therefore

$\frac{1.57}{0.0693}$  † or 22.7.

As the vapour of alcohol is 22.7 times heavier than hydrogen, the molecular weight of which is 2, the molecular weight of the substance is

$$22.7 \times 2 = 45.4.$$

This number is more simply obtained by multiplying the specific gravity of the vapour by 28.86 (= 2/0.0693).

$$0.0396 = 34.0 \times \frac{735}{760} \times \frac{273}{293} \times 0.001293;$$

0.001293 = weight of 1 c.c. of air at 0° and 760 mm.; pressure of water vapour at 20° = 17 mm.

† 0.0693 = specific gravity of hydrogen referred to air.

There are other methods of determining vapour density, of which the chief are Dumas', in which a known volume of the vapour is actually weighed, and Hofmann's, in which the volume of a known weight is directly measured; but they are now little used.



Fig. 4. — Determination of Vapour Density by Air-Displacement method.

**13. Determination of Molecular Formula from Vapour Density.**—A molecular formula is either identical with the empirical formula, or an exact multiple of it. The sum of the atomic weights given by the empirical formula  $C_2H_6O$  is 46; the molecular weight of alcohol is therefore either 46, or a multiple of this, such as 92 or 138. The number 45.2 calculated from the vapour density, although not actually coincident with any of these, is so near the first that this is evidently the actual molecular weight.

The determination of vapour density does not give such accurate results as analysis; the molecular weight calculated from it is used as an index, and must not be taken as the actual value.

The formula



Molecular Formula of Alcohol.

therefore represents the actual number of atoms in the molecule, as well as the relative numbers of the atoms in any particular portion of the substance (Gerhardt and Laurent, 1845). It is termed a molecular formula.

The molecular formula here happens to be identical with the empirical formula, but this is not always so; the molecular formula of acetic acid is double, and that of benzene six times the empirical formula.

**14. Other Methods of Determining Molecular Weight:—the Cryoscopic Method.**—There are various other methods of determining molecular weight. When a small quantity of a substance is dissolved in a pure liquid with which it does not interact, the freezing point of the solvent is lowered by an amount which depends on the molecular weights and relative proportions of the two substances.

The exact relation is given by the equation

$$M = KP/D \text{ (Raoult, 1882),}$$

where  $M$  is the molecular weight of the dissolved substance,  $P$  the weight dissolved in 100 grams of the solvent,  $D$  the depression of the freezing point, and  $K$  a constant for each particular solvent.

The value of  $K$  is determined either by finding the depression produced by a substance of known molecular weight, or by calculation from the formula

$$K = T^2/50L,$$

where  $T$  is the freezing-point of the solvent in absolute temperature, and  $L$  its latent heat of fusion (Van't Hoff, 1887); for water  $K$  is 19, for acetic acid, 39, and for benzene, 49.

It is usual to measure the depression with a special thermometer graduated in hundredths of a degree (Beckmann, 1888). Approximate results can be obtained with an ordinary physical thermometer graduated in fifths or tenths of a degree, and reading by estimation to fiftieths or hundredths.

The calculation is simple. Thus

dissolved in 0.492 gram of alcohol  
26.8 grams of water,  
lowered its freezing point from  $0^\circ$  to  $-0.79^\circ$ .

From this it follows that the molecular weight is

$$M = \frac{19 \times \frac{0.492}{26.8} \times 100}{0.79} \text{ or } 44.$$

This result is used as an index, in the same way as that calculated from the vapour density. The cryoscopic method is of great value when the substance is not volatile. It is really an adaptation of the vapour density method to solutions, for dissolved substances follow Avogadro's law in the same way as gases (Van't Hoff, 1887). Equal volumes of solutions having the same (osmotic) pressure and the same temperature contain equal numbers of molecules, and it has been shown that the osmotic pressure of a dissolved substance is proportional to the depression of the freezing point of the solvent.

An analogous method, based on the fact that the boiling point of a pure liquid is raised by the addition of a soluble substance, is also occasionally used (see Appendix, § 14). There are also various chemical methods of determining molecular weight, which will be dealt with as occasion arises.

**15. Synopsis.**—Pure alcohol is constant in chemical composition, and represented by an empirical formula  $C_2H_5O$ : from its vapour density and freezing point of its aqueous solution this formula is also the molecular formula.

## CHAPTER III

### CHEMICAL NATURE OF ALCOHOL

**16. Action of Sodium on Alcohol: Sodium Ethoxide.**—When some clean sodium is placed in absolute alcohol, a vigorous action commences, the metal being dissolved, and hydrogen given off, as when it is thrown on water. The liquid becomes viscid, and after a time ceases to dissolve the sodium when heated; and if now cooled, the product sets to a semi-solid crystalline mass.

To obtain the crystals free from the brownish mother-liquor, the pasty mass is transferred to a plate of white, unglazed earthenware. The adherent mother-liquor is rapidly absorbed by the porous earthenware, and after picking out any globules of sodium with forceps, the crystals are at once detached with a blunt spatula, and placed in a dry, well-stoppered vessel. Care should be taken to drain away mother-liquor before transferring the crystals to the plate, or the whole of the liquid may not be absorbed.

The crystalline mass, although dry, still contains alcohol, for when it is heated in a large test-tube at  $180^{\circ}$ , most conveniently by means of a bath of melted paraffin-wax, alcohol is given off, and a white residue is left. A current of dry hydrogen or coal-gas should be passed through the tube, to prevent oxidation by the air.

The residue is known as sodium ethoxide. The original crystalline product contains the alcohol as alcohol of crystallisation, analogous to water of crystallisation. *Sodium ethoxide*,  $C_2H_5.O.Na$ , is a white, amorphous, very deliquescent powder, which is decomposed when heated. *Sodium ethoxide alcoholate*,  $C_2H_5.NaO, 3C_2H_5O$ , is a colourless, crystalline substance, which is also deliquescent.

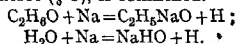
**17.—Analysis of Sodium Ethoxide: Detection of Carbon and Hydrogen in Uninflammable Compounds.**—As the ethoxide is

decomposed when heated, the only criterion of purity is constancy of composition. The substance does not burn, but the presence of carbon and hydrogen is proved by heating it to redness with some dry copper oxide in a test-tube. Carbon dioxide is evolved, and may be identified by passing the gas into a little lime-water; and steam is also given off. The residue which remains when the ethoxide is heated on platinum foil is sodium carbonate, so that sodium is present.

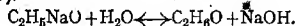
The percentage of sodium is determined by weighing the carbonate, or by converting it into sodium sulphate, and weighing this. The percentage of carbon and hydrogen is determined by combustion, as in the case of alcohol, but the substance must be mixed in the boat with some dry, powdered potassium dichromate, to decompose the sodium carbonate, the retention of carbon in which would otherwise vitiate the analysis.

The empirical formula calculated from the analytical results is  $C_2H_5NaO$ , and the percentage of alcohol given off by the crystalline alcoholate agrees with the formula,  $C_2H_5NaO, 3C_2H_6O$ .

The molecular formula of sodium ethoxide is, strictly speaking, unknown, for the substance is not volatile, and is decomposed by available solvents, but in the absence of evidence to the contrary, it is assumed to be the same as the empirical formula. Sodium ethoxide is therefore derived from alcohol in the same way as sodium hydroxide from water, namely, by substitution of a sodium atom for a hydrogen atom, and the general analogy between alcohol and water, which was indicated at the outset (§ 8), is confirmed.



**18. Hydrolysis of Sodium Ethoxide: Rational Formula of Alcohol.**—Although sodium ethoxide is deliquescent like sodium hydroxide, and apparently very soluble, it cannot be recovered from the solution, for it is decomposed by water into alcohol and caustic soda. The action is to a certain extent reversible, as some sodium ethoxide and water are formed when caustic soda is dissolved in absolute alcohol (compare § 26).



A decomposition such as this, in which a molecule is resolved into two simpler molecules by assimilating a molecule of water, is termed a *hydrolysis*—literally, a splitting by water (Armstrong, 1879). Hydrolysis must be carefully distinguished from hydration, in which water is taken up without



causing disruption of the molecule. The conversion of quicklime into slaked lime and of sulphur trioxide into sulphuric acid, are cases of hydration, whilst the conversion of phosphorus pentachloride into phosphoric acid and hydrochloric acid is a hydrolytic action.

The interconvertibility of alcohol and sodium ethoxide, taken in conjunction with the fact that sodium has no further action on the ethoxide, leads to the conclusion that in the alcohol molecule, as in the molecule of water, one of the hydrogen atoms is more easily displaced than the others. This result is conveniently summarised in a special formula,



First Rational Formula of Alcohol

in which the active hydrogen atom is placed apart from the others. Such a formula is termed a rational formula (Berzelius, 1825), because it indicates a chemical relation of the substance, namely, its analogy to water.



19. Isolation and Recognition of Small Quantities.—In studying such compositions as that of sodium ethoxide, it is unnecessary as a rule to

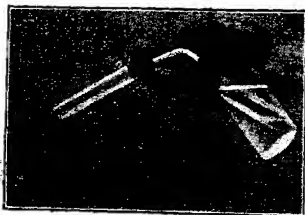


Fig. 5.—Distillation of Small Quantities.

use large quantities of material, provided that suitable apparatus is employed. A few cubic centimetres of the ethoxide solution may be distilled from a test-tube, fitted with a cork and bent delivery tube; this leads to a second test-tube, which is kept cool in a small beaker of water; a support is unnecessary, as with a little practice the whole can be held in the hand (Fig. 5).

The distillate can then be tested qualitatively. Thus the small quantity of alcohol obtained from the ethoxide solution in the above operation can be quickly converted without further purification into three substances, iodoform, aldehyde and ethyl acetate (§§ 74, 82, 39), which are recognised by their appearance or odour. No other substance yields all of these. If enough material is available, the qualitative results should be confirmed by isolating the substance itself. The alcohol in the distillate from two or three grams of sodium ethoxide may be separated by taking advantage of its insolubility in strong caustic soda solution. The liquid is slowly redistilled, and fragments of caustic soda are dissolved in the first fraction until a layer of alcohol is seen floating on the surface. The solution must be kept cool. The alcohol thus salted out may now be removed with a fine pipette, and its boiling point roughly determined in

a small test-tube, which is provided with a loosely-fitting cork holding a thermometer.

**20. Action of Phosphorus Halides on Alcohol: Ethyl Bromide and Iodide.**—The analogy of alcohol to water is confirmed by its interaction with the phosphorus halides. When bromine is slowly added to red phosphorus immersed in absolute alcohol, the phosphorus pentabromide which is formed acts energetically on the alcohol, and much heat is evolved. The action proceeds with explosive violence, if the liquid is not cooled to the ordinary temperature before each addition of bromine; but on the other hand it does not take place at all if the cooling is carried too far. On distilling the red and turbid product from a water-bath after the lapse of some hours, a volatile liquid, ethyl bromide, passes over, having a faint odour of garlic. Syrupy phosphoric acid and some unchanged phosphorus remain in the flask.



Fig. 6.—Separatory Funnel.

The liquid is impure, and contains unchanged alcohol and hydrogen bromide, as well as secondary products, but as ethyl bromide is insoluble in dilute alkalis, these may be removed by shaking it in a tap-funnel (Fig. 6) with cold dilute caustic soda. The alcohol and acid dissolve in the alkali, while the heavy ethyl bromide falls to the bottom, whence it is drawn off through the tap. If a tap-funnel is not available, a stoppered cylinder or corked test-tube may be used, the bromide being drawn off with a pipette.

The only impurities now remaining are the dissolved water, and a small quantity of a secondary product containing phosphorus. The water, which renders the liquid turbid, is removed by leaving a few small pieces of recently fused calcium chloride in it for some hours, and the trace of high-boiling phosphorus compound is then eliminated by fractionation.

The action of phosphorus and iodine on alcohol is similar, but not so violent. The iodine is dissolved in the alcohol, the calculated quantity of red phosphorus added, and after the first action is over, the whole product is gently boiled on a water-bath for an hour, with reversed condenser. Next day the crude ethyl iodide is distilled from a water-bath, and purified in the same way as the bromide.

*Ethyl bromide*,  $\text{CH}_3\text{CH}_2\text{Br}$  (Serullas, 1829), is a liquid of

ethereal but garlic odour; it boils at  $38^{\circ}$ , and has a specific gravity of 1.450 at  $15^{\circ}$ .

*Ethyl iodide*,  $\text{CH}_3\text{CH}_2\text{I}$  (Gay-Lussac, 1835), is a heavy, colourless liquid, having a pleasant ethereal odour. It boils at  $72^{\circ}$ , and has a specific gravity of 1.943 at  $15^{\circ}$ . It is less stable than the bromide, and when exposed to light turns brown from liberation of iodine.

**21. Detection and Estimation of Halogen.**—In common with most organic halogen compounds, ethyl bromide and iodide burn with a green-mantled flame when mixed with alcohol, and the presence of halogen can also be demonstrated by bringing a fragment of copper oxide moistened with either liquid into a Bunsen flame, when the volatilised copper halide tinges the flame bright green. The halogen is estimated by conversion into the silver salt.

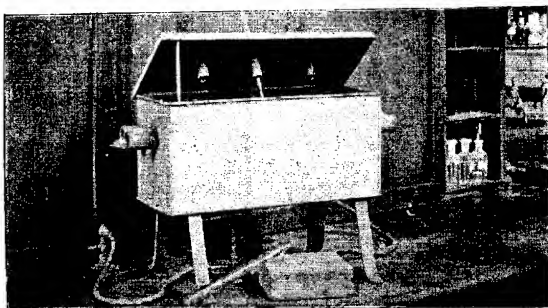


Fig. 7.—Tube-Furnace and Sealed Tubes.

The substance, which is weighed in a small bulb, is heated with the strongest nitric acid and silver nitrate for some hours, at a high temperature. The carbon and hydrogen are completely oxidised to carbon dioxide and water, and the bromine unites with the silver, forming silver bromide (Carius, 1865).

To attain the necessary temperature ( $150$ – $250^{\circ}$ ), the substance and agents are sealed up in a hard glass tube about twelve inches long, which is enclosed in a strong iron tube to minimise danger from explosion, and heated in an air-bath (Fig. 7); the complete oxidation requires several hours. When the tube has cooled, it is wrapped in a cloth, and the drawn out end is softened in a flame to allow the carbon dioxide and oxides of nitrogen to escape. The end having been cut off, the acid solution is diluted, and the silver precipitate washed, dried and weighed. The percentage of bromine is then calculated.

An analysis of ethyl bromide gave the following results—

0.2336 gram gave 0.2364 gram  $\text{CO}_2$  and 0.1248 gram  $\text{H}_2\text{O}$ ;

0.2318 gram gave 0.3987 gram  $\text{AgBr}$ .

Owing to the presence of the halogen a modification of the carbon combustion is necessary. A long roll of red-hot silver gauze is placed after the copper oxide to decompose the volatile copper bromide, some of which might otherwise pass into the calcium chloride tube and be weighed as water. The same end may be attained by substituting lead chromate for the oxide.

The percentage composition calculated from the above figures is

$$\text{C} = 21.96, \text{H} = 4.72, \text{Br} = 73.20,^*$$

from which the empirical formula of ethyl bromide is



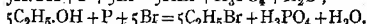
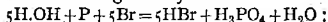
as the vapour density of the substance is 3.78, this is also its molecular formula. The percentage composition required by this formula is

$$\text{C} = 22.02, \text{H} = 4.59, \text{Br} = 73.39,$$

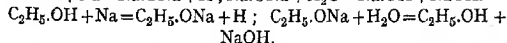
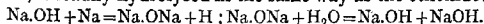
which agrees well with the above analysis.

## 22. Relation of Ethyl Bromide and Iodide to Alcohol: Second Rational Formula.—

The preparation of ethyl bromide is strictly parallel to the familiar method of preparing hydrogen bromide, by dropping bromine on red phosphorus moistened with water; in each case a hydrogen and an oxygen atom are replaced by the halogen. The formation of halogen compounds from alcohol by interaction with phosphorus halides thus not only confirms its analogy to water, but also suggests that it is an organic hydroxide.



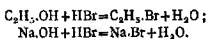
The decomposition of sodium ethoxide by water both confirms and amplifies this conclusion, for although sodium hydroxide is not decomposed in this manner, the sodium oxide (or sodium sodoxide), which is formed by the action of sodium on it, is readily hydrolysed in the same way as the ethoxide.



The resemblance of alcohol to metallic hydroxides thus indicated is borne out by its conversion into salts by the halogen acids themselves. On distilling alcohol with potassium bromide and concentrated sulphuric acid, ethyl bromide passes over, affording perhaps the easiest method of preparing this substance; whilst when alcohol is saturated with gaseous hydrogen iodide and heated, or even mixed at a low temperature with the liquefied gas, ethyl iodide is formed. Similarly the analogous ethyl

$$\frac{0.3987 \times \frac{\text{Br}}{\text{AgBr}} \times 100}{0.2318}$$

chloride is slowly formed by the direct action of hydrochloric acid on alcohol (§ 23).



The hydroxidic character of alcohol is finally established by the complete hydrolysis of ethyl bromide to sodium bromide and alcohol when boiled with caustic soda solution.

The conversion is only slowly effected, and to prevent the escape of the volatile liquids the hydrolysis is carried out in a reflux apparatus (Fig. 8).

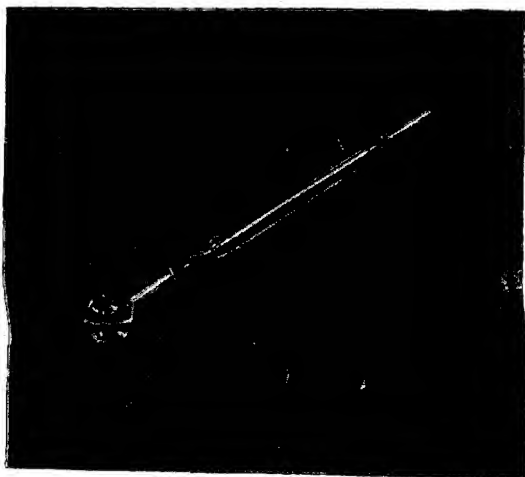
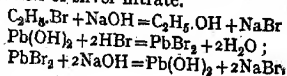


Fig. 8.—Reflux Apparatus.

or flask furnished with an inverted condenser, which condenses and returns the vapours (Frankland, 1848). The boiling is continued until the odour of the bromide is no longer perceptible on disconnecting the flask. The alcohol is then distilled off, the sodium bromide remaining with the excess of alkali and the water.

Alcohol and its bromide here behave in much the same way as the hydroxide and salt of a heavy metal, such as lead. Similarly ethyl iodide, like cadmium iodide, gives an abundant precipitate of silver iodide when shaken with a strong solution of silver nitrate.



The whole behaviour of alcohol may be summarised in the statement that it is a feebly basic hydroxide, intermediate in properties between water and sodium hydroxide; it may therefore be represented by a rational formula—



Second Rational Formula of Alcohol.

in which the hydroxyl group is placed apart from the remaining atoms. This formula includes the first rational formula; the hydrogen of ethyl bromide is not replaceable by sodium, and the active hydrogen of alcohol is therefore that which is eliminated as hydroxyl.

**23. Ethyl Chloride.**—Alcohol forms salts with most acids. Ethyl chloride, a very volatile liquid resembling the bromide, is made by direct interaction with the gaseous acid. If a saturated solution of hydrogen chloride in absolute alcohol be kept in a sealed vessel for some years, the liquid slowly separates into two layers, the upper of which is ethyl chloride. The gradual diminution in the amount of acid present can also be followed by titration. The rate of action is enormously accelerated by raising the temperature, and at the same time removing the water by means of a dehydrating agent such as zinc chloride (Groves, 1874).

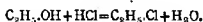
The spirit is boiled with anhydrous zinc chloride in a reflux apparatus in an oil-bath, while dry hydrogen chloride is passed into the mixture. Unattacked alcohol is returned by the condenser, whilst the ethyl chloride vapour passes from the upper end. After traversing wash-bottles of warm water and dilute alkali, to remove hydrochloric acid and alcohol, and of strong sulphuric acid, to remove alcohol and water, it is condensed in a freezing mixture. The zinc chloride retains the liberated water (see also § 106). Ethyl chloride may also be made by warming a mixture of alcohol, common salt and concentrated sulphuric acid.

*Ethyl chloride*,  $\text{CH}_3\cdot\text{CH}_2\text{Cl}$  (Basil Valentine, sixteenth century, "spirit of salt and wine"), is a liquid, which resembles the bromide in odour, but boils at  $12^\circ$ , and has a specific gravity of 0.921 at  $0^\circ$ . As a halogen compound it burns with a green-mantled flame. On account of its volatility, it is usually preserved in sealed tubes; but it may be kept in a cool place in well-stoppered bottles, provided with well-ground glass caps (Fig. 11, § 34).

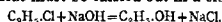
Ethyl chloride is formed in large quantities as a bye-product in the manufacture of chloral (§ 115), and is used in dentistry and minor operations both as a local or refrigerating anæ-

thetic, and as a rapid, temporary anæsthetic in place of nitrous oxide.

The analysis and vapour density of ethyl chloride lead to the empirical and molecular formula  $C_2H_5Cl$ ; the chlorine is detected and estimated in the same way as bromine or iodine. The action of hydrochloric acid thus resembles that of hydrobromic acid, the alcohol again behaving as a basic hydroxide.



This is further confirmed by the hydrolysis, which on account of the volatility of the chloride must be carried out in a closed vessel.



**24. Synopsis.**—In its actions with sodium, the halogen acids, and the phosphorus halogen compounds, alcohol behaves as a feebly basic hydroxide, intermediate to water and caustic soda. It may therefore be represented by the rational formula  $C_2H_5.OH$ . The halogen derivatives form a graduated series.

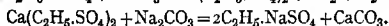
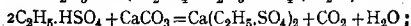
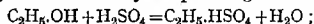
Ethyl Halides	Boiling-point	Sp. gr. at $0^\circ$
Fluoride	$-32^\circ$	Gas
Chloride	$+12^\circ$	0.921
Bromide	$+36^\circ$	1.496
Iodide	$+72^\circ$	1.979

## CHAPTER IV

### THE ETHYL RADICAL

**25. The Ethyl Sulphates.**—The basic character of alcohol is well illustrated by the existence of two ethyl sulphates, an acid salt and a normal salt. The acid salt, ethyl hydrogen sulphate, is readily formed by the direct action of sulphuric acid on alcohol, and is conveniently isolated as a sodium derivative, ethyl sodium sulphate.

A mixture of alcohol and strong sulphuric acid is heated in an open flask on a water-bath for an hour. The ethyl hydrogen sulphate is cooled, diluted with water, and neutralised in a large basin with a thin cream of calcium carbonate. The ethyl calcium sulphate (which is freely soluble, although a compound of calcium and sulphuric acid) is then converted into the sodium salt by cautiously adding sodium carbonate solution to the clear filtrate as long as a precipitate is formed. The solution of ethyl sodium sulphate, which should be just alkaline, is boiled down to one-fourth, and then evaporated on a water-bath until it begins to crystallise. After some hours, the crystals are drained, and dried on a porous plate. A further quantity may be obtained by evaporating the mother liquor.



After the crude ethyl hydrogen sulphate has been neutralised with calcium carbonate, the calcium sulphate forms a thick cream, from which the liquid cannot be completely separated by ordinary filtration. It is best in such cases to remove as much of the precipitate as possible by pouring the cream on a square of calico supported by a large funnel. The edges of the calico are gathered together, and the mass is squeezed dry; the removal of the last portions of liquid requires a press. The turbid solution is then filtered in the ordinary manner, or better, with the aid of a filter-pump and Buchner porcelain funnel (Fig. 9). This funnel has a perforated false bottom, to take a disc of filter-paper; it is fitted to the neck of a stout flask (an ordinary flask would collapse) which is



connected with the vacuum pump through a side-tube. As an alternative, an ordinary funnel may be employed containing a small perforated disc of porcelain or a perforated cone of waxed paper; a folded filter is used in the latter case.

*Ethyl sodium sulphate*,  $C_2H_5NaSO_4$ , crystallises with water in silky masses, having a pleasant odour and sweetish taste; it may be recrystallised from hot alcohol. *Ethyl calcium*

*sulphate* is similar:

*Ethyl hydrogen sulphate* or *sulphovinic acid*,

$C_2H_5HSO_4$  (Dabit,

1800), is obtained by

exactly precipitating

the metal with dilute

sulphuric acid from a

solution of the calcium,

or better, the

barium salt. The clear

filtered solution is

evaporated in a vacuum

at the ordinary

temperature, over

strong sulphuric acid,

as the sulphate is decomposed

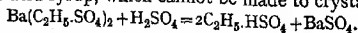
by hot

water. After some

days the organic salt

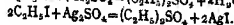
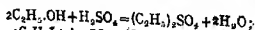
remains as a thick,

colourless acid syrup, which cannot be made to crystallise.



The second or normal salt, diethyl sulphate, is formed in small quantity in the preparation of the acid salt, and can be extracted with ether (§ 85) from the mother-liquor of the ethyl sodium sulphate. It is also formed by heating ethyl iodide with silver sulphate in a sealed tube. It is most readily obtained by extracting with chloroform a mixture of alcohol and excess of sulphuric acid; the temperature of which has not been allowed to rise above  $6^\circ$ .

*Ethyl sulphate* or "oil of wine,"  $(C_2H_5)_2SO_4$ , is a heavy, colourless liquid, which boils at  $208^\circ$ , and has a characteristic fragrant odour.



The presence of sulphur in these ethyl sulphates is proved by heating them to redness with sodium, when sodium sulphide



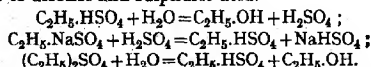
Fig. 9.—Buchner Funnel.

is formed; on adding lead acetate to the aqueous extract of the product a black precipitate of lead sulphide is therefore obtained.

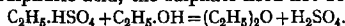
The sulphur is estimated as barium sulphate. The substance is completely oxidised by heating it with concentrated nitric acid in a sealed tube, in the same way as in the estimation of halogen. The sulphuric acid thus formed is precipitated from the diluted product with barium chloride, the barium sulphate being collected and weighed.

The empirical formulæ indicated by the analyses of the sodium and hydrogen salts are those used above, and the molecular formulæ are assumed to be the same. The molecular formula of the diethyl salt follows from its vapour density.

The ethyl sulphates are hydrolysed much more readily than the halogen salts. On simply boiling ethyl hydrogen sulphate with water, it is resolved into alcohol and sulphuric acid (Hennell, 1821). Ethyl sodium sulphate is stable in neutral or alkaline solution, but is converted by acids into ethyl hydrogen sulphate. When warmed with the slightest excess of acid it is therefore hydrolysed to sodium sulphate and alcohol. Diethyl sulphate is hydrolysed by cold water to ethyl hydrogen sulphate and alcohol, and by warm water therefore to alcohol and sulphuric acid.



**26. Ethyl Oxide: Common Ether.**—The hydroxidic character of alcohol is further evidenced by the existence of the corresponding oxide, common ether. Ether is formed by heating ethyl hydrogen sulphate with alcohol instead of with water, and as the action proceeds equally well in presence of excess of sulphuric acid, the sulphate need not be isolated.



The mixture of alcohol and strong sulphuric acid is heated at  $140^\circ$ , when it boils. Ether and water pass over, and by running in more alcohol at such a rate as to maintain the temperature constant (Fig. 10) a continuous stream of the two products is obtained.

Theoretically there should be no end to the action, as the sulphuric acid, which is continuously regenerated, acts on a further portion of the alcohol, forming more ethyl hydrogen sulphate. In practice, owing to secondary actions, the mixture soon becomes charred; the water also tends to accumulate, hydrolysing the ethyl hydrogen sulphate, and causing an increasing amount of alcohol to pass over. The operation has therefore to be started afresh when about four times the original volume of alcohol has been added.

The distillate contains sulphurous acid and alcohol in addition to ether and water; these impurities are withdrawn by shaking successively with dilute caustic soda, and strong calcium chloride solution, until the washings, separated by means of a tap-funnel, cease to give the iodoform reaction for alcohol. The light, insoluble ether rises to the surface each time. Finally, after separating from the wash-liquid, it is dried with fused calcium chloride, and redistilled from a water-bath, in contact with a little sodium. The last traces of alcohol can only be eliminated by oxidation with chromic acid; when quite free from alcohol, ether does not dissolve aniline violet.

*Ethyl oxide* or *ether* \*,  $(C_2H_5)_2O$ , (Valerius Cordus, 1542), is an



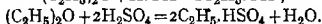
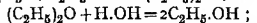
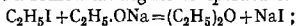
Fig. 10. Continuous Ether Process.

extremely mobile and volatile liquid, having a very characteristic odour. It boils at  $35^\circ$ , and the frozen solid melts at  $-113^\circ$ ; the specific gravity is 0.736 at  $0^\circ$ . Ether is a valuable solvent for fats, resins, and other substances which are insoluble in water, and is therefore much used in the laboratory. It is also used as an anæsthetic, both by inhalation and locally as a refrigerant. The vapour is dangerously inflammable, and must never be brought near a naked flame.

The percentage composition and vapour density of ether

\*  $air/\rho$  = the attenuated upper air; hence "attenuated" spirit.

lead to molecular formula,  $C_4H_{10}O$ . Its rational formula as ethyl oxide,  $(C_2H_5)_2O$ , is proved by its formation when ethyl iodide is heated with sodium ethoxide in a sealed tube, or dissolved in a concentrated alcoholic solution of sodium hydroxide (Williamson, 1851; compare § 18). The formula is confirmed by the hydrolysis of ether to alcohol when heated with dilute sulphuric acid in a sealed tube at  $150^\circ$ ; and by its conversion into ethyl hydrogen sulphate by concentrated sulphuric acid at a somewhat higher temperature.



Dilute acids, alkalies, sodium and phosphorus pentachloride have no action on ether at the ordinary temperature; but it is converted into ethyl chloride when heated with the pentachloride.

**27. The Ethyl Radical: Alkylie Hydroxyl.**—The derivatives of alcohol are thus, on the one hand, parallel to those of water, and, on the other hand, to those of sodium hydroxide, and the sodium and hydrogen atoms and the atomic group,



The Ethyl Radical.

are combined with and interchange the same groups or atoms, and pass unchanged through the various transformations. The organic group behaves throughout as a weak basic radical, analogous to the metallic radicals (Liebig, 1834). Were it not that it can be oxidised to carbon dioxide and water, it might be regarded as an organic element.

#### SODIUM, ETHYL, AND HYDROGEN COMPOUNDS.

Na.OH	$C_2H_5.OH$	H.OH
Na.ONa	$C_2H_5.ONa$	H.ONa
Na.Br	$C_2H_5.Br$	H.Br
Na.Cl	$C_2H_5.Cl$	H.Cl
Na.HSO <sub>4</sub>	$C_2H_5.HSO_4$	H.HSO <sub>4</sub>
Na <sub>2</sub> SO <sub>4</sub>	$(C_2H_5)_2SO_4$	H <sub>2</sub> SO <sub>4</sub>
Na <sub>2</sub> O	$(C_2H_5)_2O$	H <sub>2</sub> O

On account of its persistence and stability, this group is assigned a special name, ethyl\* (Liebig, ether and  $\eta$  = stuff, matter), and a special symbol, Et, so that the formula of alcohol as *ethyl hydroxide* becomes

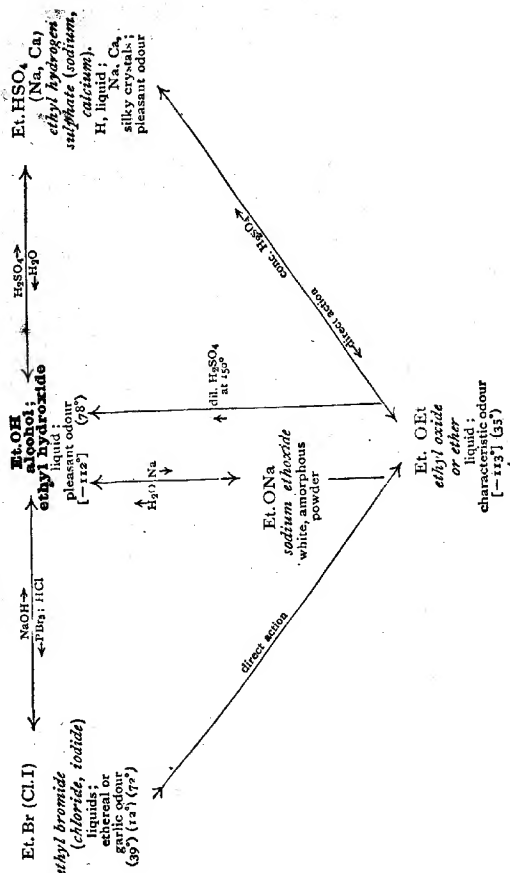


Third Rational Formula of Alcohol.

and those of its derivatives,  $\text{Et.ONa}$ ,  $\text{Et.Br}$ ,  $\text{Et}_2\text{O}$ , etc. Further, on account of the functional analogy of the ethyl radical to the alkali metals, it is termed an alkyl radical; and the hydroxyl with which it is associated is known as alkylic or alcoholic hydroxyl. Radicals play so important a part in Organic Chemistry that it was termed at one time the Chemistry of Compound Radicals (Berzelius).

**28. Synopsis.**—Alcohol is the hydroxide of a basic or alkylic radical ethyl,  $\text{C}_2\text{H}_5$  or  $\text{Et}$ , which is analogous to the alkali metals in function, and forms organic salts with the mineral acids. To indicate this, its formula is written as  $\text{C}_2\text{H}_5.\text{OH}$  or  $\text{Et.OH}$ . The corresponding oxide is common ether.

## ALCOHOL AND THE ETHYL RADICAL



*Explanation of signs used in the chart.*—A long arrow indicates that the substance to which it points can be made from the substance at the other end of the arrow. A double-headed arrow signifies that the two substances are interconvertible. The small symbols attached to arrows indicate the agents by which the changes are effected. Boiling-points are placed in curved brackets, freezing-points in square brackets.

## CHAPTER V

### PREPARATION AND COMPOSITION OF ACETIC ACID

**29. Oxidation of Alcohol to Acetic Acid: Vinegar and Wood Vinegar.**—Although alcohol resembles water and sodium hydroxide in so many respects, it differs radically from these compounds in that it is convertible into a substance having marked acid properties. It has long been known that wine and beer become sour on exposure to air and warmth; the vinegar thus generated was in fact the only acid with which the ancients were acquainted (*ζέος*, *acetum* = vinegar; *ὀξύς*, *acidum* = sharp). The mechanism of the change thus brought about was not understood in ancient times, but the process is now known to be one of oxidation; the oxygen gradually disappears from the adjacent air, and the change is equally well effected by ordinary oxidising agents (Lavoisier, 1794).

When alcohol is boiled in a reflux apparatus with potassium permanganate and dilute sulphuric acid, the permanganate is decolorised, and on distilling the product after the action has ceased, a liquid passes over, which has the sharp, characteristic odour of vinegar, and an acid reaction and taste. It is identical with distilled vinegar.

Vinegar is always made by the natural oxidation of alcohol, whilst the acetic acid used for chemical and industrial purposes is usually made by the distillation of wood.

In warm climates, wine is simply added to hot, strong vinegar in casks provided with air holes. Under the influence of the ferment (§ 172), the wine is gradually oxidised by the air, and the vinegar is drawn off as required. Malt vinegar is made from fermented wort in much the same way. "White vinegar" is manufactured by oxidising dilute spirit by the quick vinegar process (Schützenberger, 1823). The spirit is allowed to trickle through perforated casks, which are filled with beech shavings impregnated with the ferment. The shavings afford an extensive oxidising surface, well exposed to the convection current of air, which is kept moving through the apparatus by the heat generated in the action.

When chips of hard wood, such as beech or oak, are heated in a retort, gases are first evolved, and then a liquid passes over. This liquid separates into two layers, a light aqueous layer of wood vinegar or *pyroligneous acid*, and a heavy insoluble layer of wood tar (sixteenth century). Charcoal remains in the retort.

Pyroligneous acid is simply impure acetic acid (Fourcroy and Vauquelin, 1800). It is roughly distilled to separate the accompanying wood spirit (§ 43), and then neutralised with milk of lime. After the calcium acetate has been evaporated to dryness, and heated at 200° to carbonise tarry matter, it is distilled with the calculated quantity of hydrochloric acid.

**30. Purification of Acetic Acid: Crystallisation: Glacial Acetic Acid.**—On distilling dilute acetic acid, the water passes over the more quickly, and by careful fractionation a fairly strong product can be obtained (Basil Valentine, sixteenth century).

In a somewhat analogous manner, on freezing the dilute acid, the solvent water separates as ice, whilst the dissolved acetic acid remains in solution (Stahl, 1697). In this case also the process has its limits, for at a certain concentration the dissolved substance and solvent freeze together, forming an eutectic mixture, or mixture of minimum freezing-point. Conversely, the strong acid obtained by fractional distillation may itself be concentrated by freezing, the acid now being the solvent and the water remaining in solution as the dissolved substance.

In practice, however, acetic acid is concentrated by a chemical method (Stahl, 1692). The dilute acid having been neutralised with sodium carbonate and boiled to dryness, the residue is fused to expel the remaining water. (The sodium acetate first melts in its water of crystallisation, and care must be taken that this is driven off, and that a second fusion, namely of the anhydrous salt, takes place.) The anhydrous crystalline mass of sodium acetate is broken up and distilled with concentrated sulphuric acid, and finally the acetic acid is redistilled with a few fragments of acetate, in order to eliminate some sulphuric acid, which is carried over mechanically in the first distillation.

The acid thus prepared is termed glacial acetic acid, as it freezes at ordinary winter temperatures. It still contains a little water, which is eliminated by a process of fractional crystallisation. A quantity of the concentrated acid is partially frozen, and the unfrozen portion having been drained off, the crystals are melted, and the whole operation repeated until the melting-point is constant. The boiling-point and specific gravity are now also constant, and the product is pure.

When comparatively large quantities are available, as in the present case, the melting point of a substance is determined by freezing it in a



test-tube, and stirring with a thermometer until it is melted. To secure uniform heating, the test-tube is placed in a beaker of liquid (in this case water) at a few degrees above the melting-point. If the substance is pure the temperature remains stationary, once some liquid has formed, until nearly all has melted; but if it is impure, the apparent melting-point slowly rises, because the percentage of impurity in the liquid diminishes as the purer solid melts (compare Cryoscopic Formula, § 14).

**31. Composition and Formula of Acetic Acid : Determination of Molecular Weight by Silver Method.**—*Acetic acid*,  $\text{CH}_3\text{COOH}$  (De Lauraguais, 1759), is a pungent, inflammable, hygroscopic liquid, or colourless, crystalline solid. It melts at  $16.7^\circ$ , boils at  $118^\circ$ , and has a specific gravity of 1.051 at  $20^\circ$ ; it is not a very strong acid, the ionisation constant being  $K=0.0018$ . The warm glacial acid burns with a blue flame to carbon dioxide and water.

Acetic acid is much more stable than alcohol, and resists the action of even chromic trioxide, so that it is used as a solvent in oxidising organic substances with this agent. By prolonged boiling with acid permanganate, however, it is oxidised to carbon dioxide and water, whilst with alkaline permanganate it yields oxalic acid.

The empirical formula of acetic acid (Berzelius, 1814) is  $\text{CH}_3\text{O}$ .

As the vapour density when determined at a sufficiently high temperature\* is about 30, the molecular weight is 60, and the molecular formula



The molecular weight indicated by the cryoscopic method varies with the concentration of the solution, owing to the varying dissociation of the dissolved acid, but the value calculated from the vapour density is confirmed by analysis of the silver salt.

The silver salts of organic acids are easily prepared and analysed, and are almost invariably anhydrous. *Silver acetate* is a white crystalline substance, which is made by dissolving the freshly precipitated oxide or carbonate in dilute acetic acid, and evaporating the filtered solution until it crystallises. When heated to redness in a porcelain crucible the carbon and hydrogen are burned, and pure silver is left. In an analysis of dry silver acetate

0.3276 gram gave 0.3412 gram of silver,  
from which the percentage of silver is  
64.67.

The empirical formula of acetic acid being  $\text{CH}_3\text{O}$ , the possible molecular formulæ are  $\text{CH}_3\text{O}$ ,  $\text{C}_2\text{H}_4\text{O}_2$ ,  $\text{C}_3\text{H}_6\text{O}_3$ , etc. Further, as the acid forms only one silver salt, whatever the propor-

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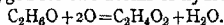
\* At temperatures near the boiling point, the molecules of acetic acid vapour are associated in pairs.

tion in which it is heated with the oxide, it is monobasic. The possible molecular formulae of silver acetate, with the corresponding percentages of silver, are therefore

Formula	Percentage of silver
CHO.Ag	78.83
C <sub>2</sub> H <sub>3</sub> O <sub>2</sub> .Ag	64.67
C <sub>3</sub> H <sub>5</sub> O <sub>2</sub> .Ag	54.82
etc.	etc.

The analysis of silver acetate shows that the second is the correct formula, and that the molecular formula of acetic acid is C<sub>2</sub>H<sub>4</sub>O<sub>2</sub>.

Acetic acid is thus derived from alcohol by the substitution of an atom of oxygen for two atoms of hydrogen.



**32. Synopsis.**—The acetic acid obtained by distillation of vinegar, and by the destructive distillation of wood, is also formed by the direct oxidation of alcohol. It has the molecular formula C<sub>2</sub>H<sub>4</sub>O<sub>2</sub>.

## CHAPTER VI

### CHEMICAL NATURE OF ACETIC ACID : THE ACETYL RADICAL

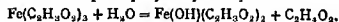
**83. The Metallic Acetates : Rational Formula of Acetic Acid.**—Acetic acid readily decomposes the alkali carbonates ; *potassium acetate*,  $K.C_2H_3O_2$ , an ill-defined, deliquescent salt, prepared in this way from the acid and carbonate (vinegar and wood ashes), was used as a medicine by the Romans. *Sodium acetate*,  $Na.C_2H_3O_2 + 3H_2O$ , melts at  $59^\circ$ , and at a higher temperature loses its water of crystallisation. *Ammonium acetate*,  $NH_4.C_2H_3O_2$ , is an extremely soluble salt, melting at  $89^\circ$ . *Barium acetate*,  $Ba(C_2H_3O_2)_2 + H_2O$ , is freely soluble in water, but insoluble in absolute alcohol. The same salts are formed by the action of the alkali hydroxides, or, in some cases, of the metals themselves on the acid.

The acetates are the oldest artificial salts. Impure *basic copper acetate* or verdigris was prepared by the Greeks as a greenish powder, by allowing grape skins to remain in contact with copper plates ; the acetic acid, which is formed by successive fermentation of the sugar, attacks the copper in presence of air. The salt is still made in essentially the same way by exposing sheet copper to the vapour of crude pyroligneous acid.

Normal *copper acetate*,  $Cu(C_2H_3O_2)_2 + H_2O$ , made by dissolving copper oxide or carbonate in the warm, dilute acid, and evaporating to crystallisation, is a well defined, dark green crystalline salt. *Lead acetate*,  $Pb(C_2H_3O_2)_2$  (Basil Valentine, sixteenth century), is prepared in a similar manner by dissolving litharge in the dilute acid ; this poisonous salt is known as sugar of lead, from its resemblance to cane sugar in appearance and taste, which, however, is also very metallic and astringent ; *basic lead acetate* is formed when a solution of the normal salt is boiled with litharge ; both salts are intermediate products in the manufacture of white lead.

The ferric acetates are used in dyeing, and are also useful in detecting small quantities of the acid. When ferric chloride is added to a neutral acetate, the solution assumes a deep red colour, owing to the formation of normal *ferric acetate*,  $Fe(C_2H_3O_2)_3$ . This is decomposed by dilute hydrochloric acid ; by simply boiling with water, it is partially hydrolysed to

an insoluble brown basic ferric acetate, part of the acid being set free. Aluminium acetate is completely hydrolysed by steam.



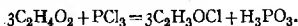
From the existence of these salts it is evident that, as in alcohol, one of the hydrogen atoms of the acetic acid molecule is more active than the others, and that the acid may be represented by a rational formula,



analogous to that of the basic hydroxide. But it is noteworthy that the unique hydrogen atom is more active than in alcohol. Sodium acetate is much more easily formed than sodium ethoxide, and conversely, more stable; it may be heated with water at any temperature without being decomposed.

#### 34. Action of Phosphorus Chlorides on Acetic Acid: Acetyl Chloride: Second Rational Formula of Acetic Acid.

—The resemblance of acetic acid to alcohol extends to its action with the phosphorus halogen compounds. When glacial acetic acid is mixed with half its volume of phosphorus trichloride, heat is evolved, and after a time the mixture separates into two layers, the upper of which consists of the chloro-derivative mixed with some unchanged trichloride, and the lower of a solution of phosphorous acid in acetic acid.



On fractionating the upper layer, which should be separated with a tap-funnel, the main fraction boils at 50–58°, the less volatile portion consisting chiefly of unchanged phosphorus trichloride, boiling at 76°. After purification by repeated distillation over small quantities of fused sodium acetate, the product boils at a nearly constant temperature; it is difficult to free it completely from phosphorus trichloride. A considerable amount of hydrogen chloride is always evolved during the preparation, even, it is said, when the acid is quite anhydrous.\*

Phosphorus pentachloride may be substituted for the trichloride, in which case phosphoric acid is formed; but owing to its solid condition, it is less easily brought into contact with the acid.

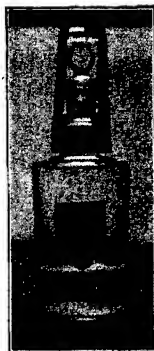
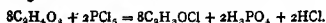


Fig. 11. Caprell bottle.  
for Hygroscopic or Volatile  
Liquids.

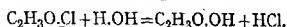
This, however, would necessitate the formation of phosphorus trioxide.

*Acetyl chloride* or *acetic chloride*,  $\text{CH}_3\text{COCl}$  (Gerhardt, 1851), is a colourless, very pungent liquid, which boils at  $51^\circ$ , and has a specific gravity of 1.130 at  $0^\circ$ ; it fumes strongly in the air, and corrodes animal and vegetable tissues. Acetyl chloride is very hygroscopic, and hence should be kept in a well-stoppered bottle, fitted with a glass cap (Fig. 11).

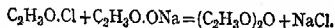
The analysis and vapour density lead to the molecular formula  $\text{C}_2\text{H}_3\text{OCl}$ ; the action of the phosphorus chlorides on acetic acid is therefore similar to that of the pentabromide on alcohol, hydroxyl being replaced by halogen. The phosphorus haloids serve to show the presence of hydroxyl, both in the alcohol and the acid; in each case the hydroxyl is replaced by halogen, whilst the haloid is converted into phosphorous or phosphoric acid.



Acetyl chloride is not only formed in the same way as ethyl bromide, but is decomposed in the same manner by hydrolytic agents, although much more readily. When poured into cold water, it at first sinks to the bottom; it soon dissolves, however, with evolution of heat, and the solution now contains acetic and hydrochloric acids. The vapour of the chloride is hydrolysed in the same way by the moisture of the air, whence the fuming of the liquid.



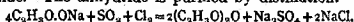
**35. Acetyl Oxide.**—As ethyl bromide and sodium ethoxide interact to form ethyl oxide, an analogous acetyl oxide may be expected from acetyl chloride and sodium acetate, the corresponding acetyl derivatives (Williamson, 1851). But acetyl oxide, although analogous to ethyl oxide in its composition and the manner of its formation, has little else in common with it; it is usually known as acetic anhydride, as it readily combines with water, forming acetic acid.



On adding acetyl chloride to powdered, recently-fused sodium acetate, there is a brisk action, which is completed by boiling the well-mixed mass for an hour or two; the operation is carried out in a reflux apparatus heated in an oil-bath. The crude anhydride, having been distilled off, is freed from traces of acetyl chloride by again boiling with anhydrous sodium acetate; on redistillation it now boils constantly, and is pure.

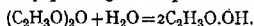
Acetic anhydride is also readily prepared by saturating anhydrous sodium

acetate with chlorine mixed with rather more than an equal volume of sulphur dioxide. The anhydride is purified by distillation.



*Acetic anhydride* or *acetyl oxide*,  $(CH_3CO)_2O$  (Gerhardt, 1853), is a colourless liquid of extremely pungent odour. It boils at  $138^\circ$ , and has a specific gravity of 1.073 at  $20^\circ$ . The empirical and molecular formula anticipated by theory is confirmed by the analysis and vapour density, and the rational formula is proved by the manner of formation and decomposition.

Like the chloride, it is hydrolysed much more easily than the corresponding ethyl compound, the decomposition being similarly effected by pouring the liquid into water.

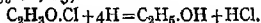


If the quantity of water is limited, the excess of the oxide remains at the bottom, as it is not affected by acetic acid, but otherwise it slowly dissolves. The hydrolysis is much hastened by warming the mixture, or by adding caustic soda solution.

**36. Indirect Reduction of Acetic Acid to Alcohol.**—Acetic acid is unaffected by ordinary reducing agents, and cannot be directly reconverted into alcohol. If, however, a little acetyl chloride or acetic anhydride is kept in contact with a large excess of sodium amalgam, in a loosely stoppered vessel, it is slowly reduced to alcohol by the hydrogen which is generated from the hygroscopic moisture.

The alcohol is separated by distilling the product, after boiling it with alkali to destroy impurities, and is readily detected in the distillate. Large quantities of anhydride are required, however, if it is desired to isolate the alcohol, the yield being very small owing to secondary actions (compare § 64).

As both acetic anhydride and acetyl chloride are so readily made from the acid, this reduction (Linneman, 1868) is practically the reversal of the oxidation of alcohol to acetic acid (compare also §§ 82, 83).



**37. The Acetyl Radical: Acetic Hydroxyl.**—From these actions it is evident that in the oxidation of alcohol it is the ethyl radical which is affected, and that it is transformed into an oxidised radical of the formula,



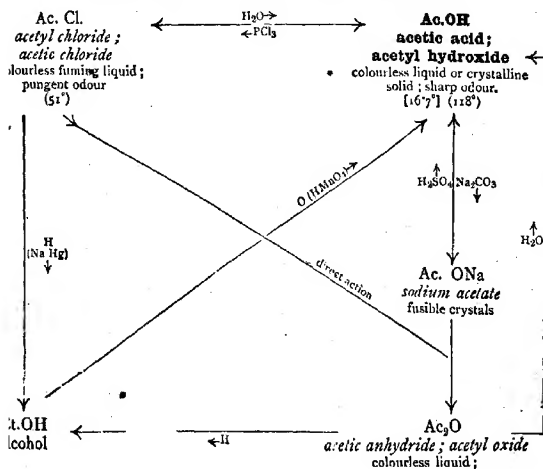
The Acetyl Radical.

two atoms of hydrogen being replaced by the equivalent single atom of oxygen.

This radical is termed *acetyl*, and assigned the symbol *Ac*, so that acetic acid is *acetyl hydroxide*. This negative radical, formed by the substitution of oxygen for hydrogen in the positive ethyl group, is analogous to the radicals of the inorganic acids. It is termed an *acidic radical*, and the hydroxyl with which it is associated is known as *acidic hydroxyl*. The hydrogen of acidic hydroxyl is more active than that of alkylic hydroxyl.

**38. Synopsis.**—From the action of acetic acid with phosphorus chloride and the mineral bases, it is the hydroxide of an acid or acyl radical, acetyl,  $C_2H_3O$  or *Ac*, analogous to the inorganic hydroxyacids, and its formula may be written as  $C_2H_3O.OH$  or *Ac.OH*. The phosphorus haloids serve to detect both alkylic and acidic hydroxyl.

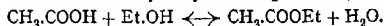
#### ACETIC ACID AND THE ACETYL RADICAL.



## CHAPTER VII

### ETHYL ACETATE

**39. Preparation of Ethyl Acetate.**—When absolute alcohol and acetic acid are mixed, they gradually combine to form a neutral compound, ethyl acetate, and the acidity of the mixture diminishes. The action is never complete, because water is formed, which hydrolyses the product (§ 40).



Equilibrium has been found to result when two-thirds of the acid and alcohol have combined, the opposed actions then proceeding at equal rates (Berthelot, 1878). At the ordinary temperature the change is exceedingly slow, and takes six years to reach equilibrium; it is rapidly accelerated as the temperature is raised, and at 100° the action is finished in a week or two. But the final proportions are the same, and are independent of the temperature.

The process of combination is greatly accelerated by adding a strong acid such as sulphuric or hydrochloric acid to the mixture (Scheele, 1782), the accelerative or catalytic action here being due to the hydrogen ions; weak acids have little or no influence on the rate of interaction.

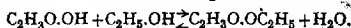
When hydrochloric acid is employed, about one-fourth of a mixture of alcohol and acetic acid in molecular proportion is saturated with hydrogen chloride gas, and mixed with the remaining three-fourths. The mixture is then boiled for an hour or two in a reflux apparatus.

The product having been cooled, the ethyl acetate is salted out by shaking the liquid with common salt and a little water. Alcohol and acetic acid are soluble in brine, but ethyl acetate is insoluble, so that the heavy layer of brine can be separated with a tap-funnel. The ethyl acetate is then shaken with a saturated solution of washing-soda, to remove the last traces of acid, and finally dried with potassium carbonate, or recently-fused sodium acetate. (Calcium chloride is unsuitable, as it is soluble in ethyl acetate.) It is then carefully fractionated. The last traces of water and alcohol can be removed by means of phosphorus pentoxide.

When sulphuric acid is used as the catalyst, the process

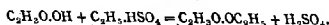


can be made continuous, as in the manufacture of ether. A mixture of ethyl acetate, alcohol and water, containing about 80 per cent. of the acetate, boils constantly at about  $70^{\circ}$ , and if alcohol and acetic acid be heated on a water-bath with a little sulphuric acid, this mixture distils as fast as the materials are introduced. The distillate is purified as above.



This is the best method of making large quantities of ethyl acetate; the apparatus is the same as that which is used in the continuous ether process (Fig. 10, § 26), substituting a water-bath for the sand-bath. The crude ethyl acetate may also be freed from alcohol fairly effectively by distilling it with an equal bulk of water from a water-bath, and washing the vapour before condensation by passage through several vessels of water at  $100^{\circ}$ . The distillate is separated from the subjacent water and dried with potassium carbonate, the residual alcohol being removed either by fractionation through a very efficient still-head (§ 4), or by treatment with phosphorus pentoxide.

Ethyl acetate can also be made directly from metallic acetates (Scheele, 1782). Coarsely powdered, recently fused sodium acetate is gradually added to a cooled mixture of alcohol and sulphuric acid, in the preparation of which heating has been avoided as far as possible. The liberated acetic acid slowly interacts with the ethyl hydrogen sulphate, and when the mass, which after a day or two is almost solid, is heated on a water-bath, fairly pure ethyl acetate passes over. The ethyl hydrogen sulphate probably interacts with the acid in the same way as with alcohol in the preparation of ether.



#### 40. Composition and Formula of Ethyl Acetate: its Hydrolysis.

—*Ethyl acetate, acetic ether or acetic ester.*\*  $CH_3.COOEt$  (De Lauraguais, 1759), is a colourless, neutral liquid, which, when pure, is akin to ordinary ether in odour. It boils at  $77^{\circ}$ , freezes at  $-84^{\circ}$ , and has a specific gravity of 0.907 at  $15^{\circ}$ . The empirical formula is  $C_4H_8O_2$ , and as the vapour density is about 4.4, the molecular formula is  $C_4H_8O_2$ , which agrees with the rational formula,  $C_2H_5O.OC_2H_5$ , anticipated from theoretical considerations.

This rational formula is also confirmed by the hydrolysis, which is readily effected by boiling the liquid with caustic soda solution in a reflux apparatus, until its odour is no longer perceptible. Alcohol can be distilled at once from the product, and acetic acid passes over on resuming the distillation after the residue has been strongly acidified with dilute sulphuric acid.

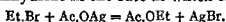
\* From German *Aether* and *Säure* (acid).

The ethereal salt is resolved into acid and alcohol, just as a metallic salt is decomposed into acid and base. The process is sometimes termed saponification, from the analogy of the action to that which is involved in soap-making (§ 48).

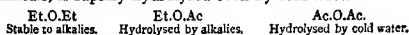


The hydrolysis is also effected, although very much more slowly, by water alone. If some neutral ethyl acetate be left in contact with a molecular proportion of water, the solution soon becomes acid, and the acidity slowly increases until one-third of the ester has been hydrolysed. The point of equilibrium is identical with that which results from the interaction of alcohol and acetic acid (§ 39), and is reached more quickly when the mixture is heated. The accelerating influence of the alkali is due to the hydroxyl ions of the soda, which combine with the ethyl radical, forming undissociated alcohol; the strength of a base can therefore be measured by its accelerating influence on the hydrolysis of ethyl acetate.

Further confirmation of the above rational formula is afforded by other methods of preparation. Thus when ethyl iodide is heated with dry silver acetate, the white acetate is converted into yellow silver iodide, and the odour of the iodide is replaced by that of ethyl acetate. The action is analogous to the formation of ether from ethyl iodide and sodium ethoxide, and to that of acetic anhydride from acetyl chloride and sodium acetate. On this account ethyl acetate may be regarded as a compound ether or double oxide of the ethyl and acetyl radicals; it is intermediate to ether and acetic anhydride in the rate at which it is hydrolysed.

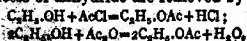


The three oxides show the same gradation in properties as the two corresponding hydroxides, and afford an excellent illustration of the influence of radicals on the activity of organic compounds. Acetic acid is more active than alcohol because of the influence of the negative acetyl radical. Ether, which contains two positive radicals, is a stable, inert substance; ethyl acetate, with one positive and one negative radical, is readily hydrolysed by alkalies; acetic anhydride, which contains two negative radicals, is rapidly hydrolysed even by cold water.



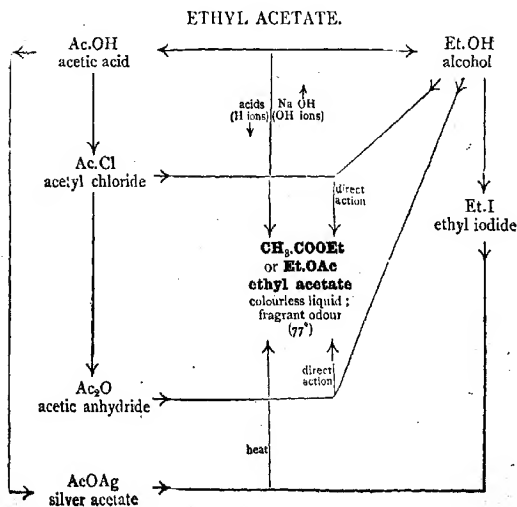
**41. Action of Acetyl Chloride and Acetic Anhydride on Alcohol : Differentiation of Alkyls from Acidic Hydroxyl.**—When acetyl chloride is mixed with absolute alcohol, there is a violent action, and much hydrogen chloride gas is evolved. On diluting the product slightly with water, and neutralising it with sodium carbonate, the odour of ethyl acetate is noticeable. The ester can be salted out by adding more of this salt, and characterised in the manner described above.

The action of acetic anhydride is similar, except that water is eliminated instead of hydrogen chloride, and that the mixture must be warmed; this is the best way of obtaining ethyl acetate free from alcohol; the acetic acid and excess of anhydride are removed by fractionation.



The acetyl radical here takes the place of the hydrogen of the alkylic hydroxyl, and as neither acetyl chloride nor acetic anhydride has any action on acetic acid, it is evident that these agents afford a means of distinguishing alkylic from acidic hydroxyl (Schützenberger, 1865). The presence of hydroxyl having been proved by the action of phosphorus pentachloride, the substance is treated with acetyl chloride. If the hydroxyl is acidic, there is no action, but if it is alcoholic, hydrogen chloride gas is evolved, often with explosive violence, and the acetate of the alcohol is formed.

**42. Synopsis.**—Alcohol and acetic acid unite to form ethyl acetate, which is analogous on the one hand to the metallic salts, and hence is termed an ethereal salt, and on the other hand to ether and acetic anhydride, and hence is termed an ester or compound ether. Acetyl chloride and acetic anhydride serve to differentiate alcoholic from acidic hydroxyl.



## CHAPTER VIII

### THE ALCOHOLS AND ACIDS OF THE ACETIC SERIES

**43. Methyl Alcohol and the Methyl Radical.**—Alcohol, acetic acid, and ethyl acetate are types of three large classes of organic compounds; the alcohols, the acids, and the ethereal salts or esters. We can now examine these in detail.

The simplest of all the alcohols is methyl alcohol, which is formed in the dry distillation of wood, and thus accompanies acetic acid in crude pyroligneous acid. The head fraction obtained in the purification of this acid is a volatile, inflammable liquid termed *wood spirit* (Boyle, 1661); it consists chiefly of acetone (§ 88) and the new alcohol, the isolation of which is a somewhat complicated process.

The crude spirit is repeatedly boiled with lime, to eliminate acetic acid and water, and hydrolyse methyl acetate, and is then fractionated to separate the acetone. When free from acetone methyl alcohol does not yield iodoform with iodine and caustic alkali, and hence is readily distinguished from ordinary alcohol.

Commercial methyl alcohol still contains some acetone, which is best eliminated by boiling with anhydrous oxalic acid, with which the alcohol forms a crystalline ethereal salt. The methyl oxalate, which separates on cooling the solution, is washed with cold water until free from acetone, and then hydrolysed. The alcohol is dehydrated over quicklime; or it may be dried by careful fractionation, as, unlike ethyl alcohol, it does not form a mixture of constant boiling-point with water.

An alternative method, which has the advantage of being less expensive, consists in boiling the commercial alcohol with anhydrous calcium chloride, which subsequently crystallises from the saturated solution as an alcoholate (§ 8). The crystalline mass is drained, and finally decomposed by heat.

The alcohol is also prepared on a large scale by the dry distillation of "vinasses," the residual liquor from the alcoholic fermentation of beet molasses (§ 213). It also occurs naturally in the oil of the winter-green, a shrub indigenous to New Jersey; the chief constituent of this oil is methyl salicylate (§ 308), an ethereal salt from which pure methyl alcohol is set free by hydrolytic agents. It is a curious fact that methyl compounds occur in natural products much more frequently than ethyl compounds.

*Methyl alcohol*,  $\text{CH}_3\text{OH}$  (Taylor, 1812), is a colourless liquid, which closely resembles ordinary or ethyl alcohol; it boils at  $65^\circ$ , freezes at  $-94^\circ$ , and has a specific gravity of 0.797 at  $15^\circ$ . It is used for the methylation of ordinary alcohol, the preparation of various aniline dyes, and the manufacture of the antiseptic, formalin (§ 86).

The chemical behaviour of methyl alcohol is similar to that of ethyl alcohol in almost every detail. Sodium dissolves in it, forming a crystalline compound, which when heated yields *sodium methoxide*,  $\text{CH}_3\text{ONa}$ , a white amorphous powder resembling sodium ethoxide. This is reconverted by water into caustic soda and the alcohol.

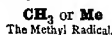
The only difference from sodium ethoxide is that it does not oxidise and turn brown in air; hence methyl alcohol is employed instead of ethyl alcohol when caustic alkalies are required in alcoholic solution.

The action of the phosphorus haloids and the acids is also similar. *Methyl iodide*,  $\text{CH}_3\text{I}$  (Dumas and Péligot, 1835), is formed in the same way as ethyl iodide; it boils at  $44^\circ$ , and has a specific gravity of 2.27 at  $15^\circ$ . *Methyl hydrogen sulphate*,  $\text{CH}_3\text{HSO}_4$ , is a syrupy liquid, and *methyl sodium sulphate*,  $\text{CH}_3\text{NaSO}_4$ , a soft crystalline solid.

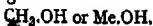
*Methyl chloride*,  $\text{CH}_3\text{Cl}$  (Dumas, 1831), formed by the action of hydrogen chloride on methyl alcohol in presence of zinc chloride, differs from ethyl chloride only in that it boils at  $-23^\circ$ , and is gaseous at ordinary temperatures. *Methyl bromide*,  $\text{CH}_3\text{Br}$  (Bunsen, 1844), is a similar volatile liquid, boiling at  $4^\circ$ ; it is hydrolysed by caustic soda to methyl alcohol and sodium bromide. *Methyl sulphate*,  $(\text{CH}_3)_2\text{SO}_4$ , from methyl alcohol and pyrosulphuric acid, is a heavy liquid which boils at  $189^\circ$ , and like ethyl sulphate is very poisonous.

*Methyl oxide or methyl ether*,  $(\text{CH}_3)_2\text{O}$  (Dumas), is a soluble gas which liquefies at  $-23^\circ$ ; it is prepared in the same way as ordinary ether, and is therefore present in ether made from methylated spirit. *Methyl acetate*,  $\text{CH}_3\text{CO.OCH}_3$ , made by the action of acetic acid on methyl alcohol in presence of strong acids, is a fragrant liquid which boils at  $57^\circ$ ; it resembles ethyl acetate in all essential points.

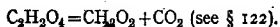
Apart from physical differences and differences of composition, everything that has been said of ethyl alcohol and its derivatives may be said of methyl alcohol and its derivatives. The simpler alcohol is therefore the hydroxide of an alkylic radical, methyl,



(Dumas and Péligot, 1834;  $\mu\epsilon\theta\nu$  = wine;  $\nu\lambda\eta$  = wood), its rational formula being



**44. Formic Acid and the Formates.**—When methyl alcohol is boiled with acid permanganate, it is partly oxidised to carbon dioxide and water, but a certain amount of formic acid, an acid oxidation product analogous to acetic acid, is also obtained. This is best prepared by distilling oxalic acid with glycerol at 120–130° (Berthelot, 1858); dilute formic acid passes over if crystallised oxalic acid is used, but eventually 90 per cent. acid if the oxalic acid has previously been dehydrated.



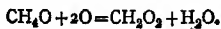
The same product is formed by exposing the alcohol to the mild oxidising action of air in presence of platinum black (Dumas, 1831); it is identical with the formic acid prepared by distilling red ants (*formicae*) or stinging nettles with water. Formic acid can also be made by distilling starch with manganese dioxide and dilute sulphuric acid (Scheele, 1770), or sugars and other carbohydrates (§ 167) with dilute mineral acids. It occurs naturally in the animal organism in certain diseases, such as rheumatic fever, in which it is probably formed by hydrolysis of lactic acid (§ 137).

Anhydrous formic acid is conveniently prepared by dehydrating the 90 per cent. acid, sp. gr. 1.2; with phosphorus pentoxide; it cannot be made by the action of sulphuric acid on the sodium salt, as it is converted into carbon monoxide by this agent. The pentoxide is cautiously added to the well-cooled acid as long as it is dissolved readily, and if care be taken to avoid rise of temperature, little decomposition occurs; on fractionally distilling the product a glacial acid is obtained, from which the last traces of water can be eliminated by fractional crystallisation.

Concentrated formic acid may also be dehydrated by boiling in a reflux apparatus with boric anhydride, but the action is very slow. A less convenient method of preparing the anhydrous acid consists in decomposing the lead salt with dry sulphuretted hydrogen at 100°.

*Formic acid*,  $\text{H.COOH}$  (Ray, 1670), is a colourless, corrosive liquid, or crystalline solid, which melts at 8°, boils at 101°, and has a specific gravity of 1.223 at 15°; a diluted acid containing 23 per cent. of water boils constantly at 107°. Formic acid is a much more powerful acid than acetic acid, its dissociation constant being 0.0214; it fumes slightly in the air, and its vapour is very pungent. The concentrated acid rapidly destroys the skin.

The empirical formula of formic acid is  $\text{CH}_2\text{O}_2$ , and this is the molecular formula indicated by the vapour density; the formation of the acid from methyl alcohol is therefore precisely analogous to that of acetic acid from ethyl alcohol, two of the methyl hydrogen atoms being replaced by an atom of oxygen.



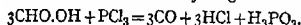
Formic acid resembles acetic acid almost as closely as methyl alcohol resembles ethyl alcohol. *Sodium formate*,  $\text{H.COONa} + \text{H}_2\text{O}$ , is a crystalline substance, resembling sodium acetate. *Ammonium formate*,  $\text{H.COONH}_4$ , is a very soluble salt resembling ammonium acetate. *Barium formate*,  $\text{Ba}(\text{CH}_2\text{O}_2)_2$ , made from the acetate and carbonate, is an important reducing agent (§ 82).

The soluble red *ferric formate*,  $\text{Fe}(\text{CHO}_2)_3$ , made in the same way as ferric acetate, is hydrolysed by boiling water in a similar manner to formic acid and an insoluble, brown, basic salt. *Copper formate*,  $\text{Cu}(\text{CHO}_2)_2 + \text{H}_2\text{O}$ , prepared from copper oxide, forms well-defined blue crystals, and *lead formate*,  $\text{Pb}(\text{CHO}_2)_2$ , also crystallises well, and is sweet and astringent like lead acetate (Ray).

*Methyl formate*,  $\text{H.COOME}$ , which is made by the interaction of sodium formate with methyl alcohol saturated with hydrogen chloride gas, is a fragrant liquid boiling at  $32^\circ$ ; like the acetate it is hydrolysed to its proximate constituents by alkalis. *Ethyl formate*,  $\text{H.COOEt}$ , is similar, but boils at  $54^\circ$ .

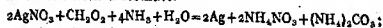
By reason, however, of their close relation to carbon monoxide and carbonic acid, formic acid and its salts behave in an anomalous manner towards oxidising and dehydrating agents. They are at once decomposed by concentrated sulphuric acid, giving a quantitative yield of carbon monoxide, and because of their ready oxidisability have marked reducing powers; formates reduce silver salts to silver in neutral solution, and mercuric chloride to calomel even in acid solution.

For the same reason the chloride and anhydride of the formyl radical  $\text{CHO}$ , of which formic acid is the hydroxide, which might be expected from the analogy to acetic acid, have never been prepared; the product of the action of phosphorus trichloride on the acid at once decomposes into carbon monoxide and hydrogen chloride.



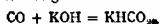
Apart, however, from this special and peculiar instability towards oxidising and dehydrating agents, formic acid is a true analogue of acetic acid.

When a solution of silver nitrate, to which enough ammonia has been added exactly to redissolve the oxide at first precipitated, is warmed with a neutral solution of a formate, metallic silver is precipitated, usually as a mirror; similarly, mercuric chloride is reduced to calomel when its solution is heated with a formate.



The conversion of formic acid into oxides of carbon is reversed with equal facility, and in this way the acid can be made artificially from its elements.

Such processes are termed synthetic processes. Potassium formate is produced quantitatively when a stick of potash is exposed to an atmosphere of carbon monoxide at  $100^{\circ}$  (Berthelot, 1855); the absorption is complete in about three days, but the same result may be brought about in an hour by passing the moist gas over soda-lime heated at  $200^{\circ}$ .



Sodium formate is also produced by the slow reduction of ammonium carbonate with sodium amalgam.



**45. Propyl Alcohol, Propionic Acid, and the Higher Alcohols and Acids.**—Several alcohols of high boiling point, which are chemically analogous to methyl and ethyl alcohol, are formed in small amount in the alcoholic fermentation of sugar. They are sparingly soluble in water, and hence form with it a milky tail fraction in the rectification of spirit; the mixture of alcohols, when separated from the accompanying water, is termed *fusel oil* (Scheele, 1785).

Although their boiling points differ considerably, these cannot be completely separated by ordinary fractionation. The mixed iodides, however, formed by the action of iodine and red phosphorus on the dry fusel oil, are convertible into the acetates by heating with silver acetate, and these acetates can be separated fractionally. The separate alcohols obtained by hydrolysing the pure acetates can then be purified and dehydrated.

*Propyl alcohol*,  $\text{C}_3\text{H}_7\text{OH}$  (Chancel, 1853), which constitutes about 3 per cent. of the fusel oil made from potato-spirit, is a liquid which boils at  $97^{\circ}$ , and has a specific gravity of 0.807 at  $15^{\circ}$ . It resembles ethyl alcohol in its chemical actions, although somewhat more sluggish, but is less pleasant in odour; and owing to the higher percentage of carbon, it burns with a luminous flame.

The various derivatives of propyl alcohol, are similar to those of ethyl and methyl alcohols, and there is no need to describe them; the only difference is that the liquid products boil at higher temperatures, and, as a rule, are denser. By the same reasoning as before, they are the compounds of a propyl radical,  $\text{C}_3\text{H}_7$  or Pr.

Propyl alcohol is readily oxidised by acid permanganate, and the resulting acid is distinguished from acetic acid by its insolubility in calcium chloride solution, by which it is salted out as an oily layer (*πρωτος πτω* = first oil). It also occurs in pyroligneous acid (§ 29), from which it may be separated by fractionation.

*Propionic acid*,  $\text{C}_2\text{H}_5\text{COOH}$  (Gottlieb, 1844), is a colourless liquid, of acid but somewhat rancid odour. The anhydrous



acid boils at  $141^{\circ}$ , freezes at  $-19^{\circ}$ , and has a specific gravity of 1.017 at  $0^{\circ}$ ; a 30 per cent. aqueous solution of propionic acid boils at  $99^{\circ}$ .

Propionic acid is a somewhat weaker acid than acetic acid, its dissociation constant being 0.0013; its derivatives are similar to those of acetic acid in the manner of their formation and decomposition, and they are therefore compounds of a propionyl radical,  $C_3H_5O$ .

Butyric acid is found as an ethereal salt in fresh butter (*butyrum*), and can be prepared from butter fat, which contains 4 or 5 per cent. of this acid. The clarified fat is heated on a water bath with alcoholic potash until it is entirely dissolved, and the heating is continued until the alcohol is expelled, water being added from time to time. The product is acidified with dilute sulphuric acid and allowed to cool, the cake of solid fat acids (§ 49) is removed, and on distilling the clear filtrate, an aqueous solution of butyric acid and allied volatile acids passes over. Butyric acid is most easily made by fermenting lactic acid (§ 136).

The butyric acid is separated from the other volatile acids by neutralising the solution with lime water. Calcium butyrate is much less soluble in hot than in cold water, and separates as a scum on heating the neutralised solution; a cold saturated solution of calcium butyrate becomes semi-solid when heated, and the acid is thus easily purified.

*Butyric acid*,  $C_3H_7COOH$  (Chevreul, 1823), is a somewhat oily liquid, having a sharp and very rancid odour. It freezes at  $-6^{\circ}$ , boils at  $162^{\circ}$ , and is only sparingly soluble in water, but readily distils with it at about  $99^{\circ}$ . The dissociation constant of the acid is 0.0015, so that it is slightly stronger than propionic acid.

The derivatives of butyric acid are similar to those of propionic and acetic acids. *Butyl alcohol*,  $C_4H_9OH$  (Lieben and Rossi, 1869), a liquid boiling at  $117^{\circ}$ , and having a distinctly unpleasant odour, forms about 6 per cent. of potato fusel oil; it was originally obtained by the reduction of butyric aldehyde (§ 86), and may also be prepared from butyric anhydride in a similar manner (§ 36).

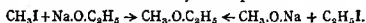
It is unnecessary to mention more than the principal of the remaining analogies of alcohol and acetic acid; acids and alcohols are known containing all numbers of carbon atoms up to eighteen, and many beyond. *Amyl alcohol*,  $C_5H_{11}OH$ , a liquid boiling at  $138^{\circ}$  (see also § 96), is related to *valeric acid*,  $C_4H_9COOH$ , in the same way as butyl alcohol to butyric acid; both the alcohol and the acid are characterised by their rank

unpleasant odours. *Caproic acid*,  $C_6H_{11} \cdot COOH$ , and *caprylic acid*,  $C_7H_{13} \cdot COOH$ , are oily liquids which occur in combination in goats' butter, and, together with butyric acid, in cows' butter. *Octyl alcohol*,  $C_8H_{17} \cdot OH$ , is found in geranium; *pelargonic acid*,  $C_9H_{17} \cdot COOH$ , in the leaves of the geranium.

**46. The Ethereal Salts and Mixed Ethers.**—The ethereal salts or esters of these alcohols and acids are liquids of fragrant odour and flavour, and in dilute alcoholic solution are used as fruit essences; they are made in the same way as ethyl acetate (§ 39). The odour and flavour of many of the fruits are due to small quantities of these substances; *propyl acetate* is characteristic of pears, the *amyl acetate* made from fusel oil recalls Jargonelle pears, and *ethyl butyrate* suggests pineapples.

Not only are the alkyl radicals variously combined with the acids in these ethereal salts, but they can be united with one another in a series of compounds, termed the mixed ethers. The existence of these completes the proof of the identity of ordinary ether with ethyl oxide (Williamson, 1851).

*Methyl ethyl ether*,  $CH_3 \cdot O \cdot C_2H_5$ , a liquid which boils at  $11^\circ$ , and resembles ordinary ether, is formed by the interaction both of methyl iodide with sodium ethoxide, and of ethyl iodide with sodium methoxide, so that the presence of both alkyl radicals cannot be doubted. Similarly, it is formed both by the action of methyl alcohol on ethyl hydrogen sulphate, and by that of ethyl alcohol on methyl hydrogen sulphate, and is therefore present in the ether made from methylated spirit.

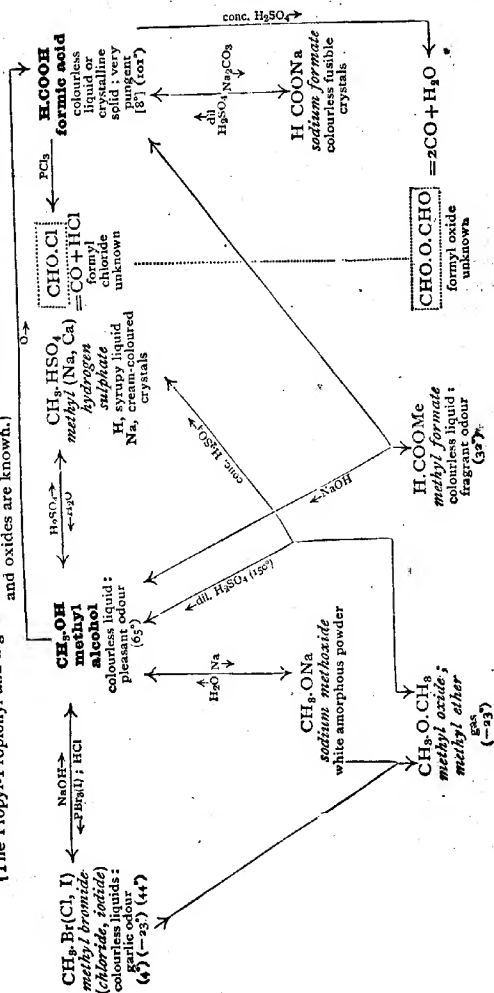


A still more convincing proof that the conversion of alcohol into ether is due to interaction with ethyl hydrogen sulphate, is afforded by the action of ordinary alcohol on a hot mixture of sulphuric acid and amyl alcohol. The mixture initially contains amyl hydrogen sulphate, and the first product is *ethyl amyl ether*,  $C_2H_5 \cdot O \cdot C_5H_{11}$ , a liquid boiling at  $112^\circ$ . But as the action proceeds, and ethyl hydrogen sulphate is formed, the mixed ether is accompanied by a steadily increasing amount of ordinary ether, until finally the latter alone passes over. The residue in the distilling flask now contains only ethyl hydrogen sulphate, which can be isolated in the customary manner (Williamson, 1851).

Besides mixed ethers, mixed acid anhydrides are known, such as *formic acetic anhydride*,  $CHO \cdot O \cdot C_2H_5O$ , and *acetic butyric anhydride*,  $C_2H_5O \cdot O \cdot C_4H_9O$ ; these are unstable liquids of high boiling-point, which are readily decomposed into their respective simple anhydrides when heated.

**47. Synopsis.**—Alcohol, acetic acid, and ethyl acetate, are types of the three classes of alcohols, acids, and ethereal salts or esters, the members of which form well-defined graduated series.

METHYL ALCOHOL AND FORMIC ACID.  
(The Propyl-Propionyl and higher charts are similar, with the addition that the acid chlorides and oxides are known.)



## CHAPTER IX

### THE FATTY ACIDS: HOMOLOGY: ISOMERISM

**48. Fats, Oils and Soaps.**—The common fats and fatty acids are ethereal salts or esters, in which a complex alcohol, glycerol  $C_3H_5(OH)_3$  (§ 127) is united with palmitic, stearic or oleic acid. *Olein*,  $C_3H_5(C_{15}H_{33}O_2)_3$  is liquid at ordinary temperatures, whilst *stearin*,  $C_3H_5(C_{17}H_{35}O_2)_3$ , and *palmitin*,  $C_3H_5(C_{16}H_{31}O_2)_3$ , are hard solids; the varying consistence of the different fats and oils depends on the relative proportions of these three constituents. The corresponding alkali salts are the ordinary soaps, and the waxes are esters of the fatty, and similar acids, with complex alcohols of the ethyl series.

Mutton suet is stearin, with some palmitin. As an ester it is readily hydrolysed by caustic soda to the alcohol, glycerol, and the sodium salt or soap; the hydrolysis of ethereal salts is hence sometimes termed saponification, the conversion of an ester into the sodium salt of its acid being analogous to the saponification (conversion into soap) of a fat.

On boiling clear, filtered fat with concentrated caustic soda solution in an iron vessel it is gradually dissolved, and, after a time, the molten globules entirely disappear; water must be added as required to replace that lost by evaporation. On stirring common salt into the product, the soap or *sodium stearate* rises to the surface as an oily layer, which solidifies to a white cake on cooling; the glycerol remains in the alkaline lye. The soap is purified by dissolving in hot water, and repeatedly salting out until sufficiently free from alkali; the cake is then allowed to dry in the air. Soap always contains a considerable proportion of water.

The hydrolysis is more rapidly effected by alcoholic soda. The fat is melted on a water-bath, and poured into alcohol, forming a granular mixture of solid and solution. Solid caustic soda is now added in small pieces; there is a violent action, which is complete as soon as the alkali has dissolved. The soap sets to a transparent cake when cold.

The impure sodium stearate obtained by boiling tallow with concentrated aqueous soda is ordinary curd soap; it derives its name from the method of purification, the soap separating in light curds when salt or strong caustic lye is added to the crude solution. Castile soap is prepared from olive oil, and the cheaper forms of curd soap are made from cocoa-nut oil, or from palm-oil, previously bleached with chromic acid mixture. Common yellow soap is prepared either from crude palm-oil,

or from tallow mixed with resin (§ 351). The transparent soaps are obtained by evaporating the alcoholic solutions of the sodium soaps, or boiling down their aqueous solutions with sugar.

Potassium soaps are more soluble than sodium soaps, and as they are converted into sodium soaps by common salt, they cannot be salted out. The highly alkaline jelly obtained by evaporating the caustic solution, is ordinary soft soap; it is usually made from train oil. Only the alkali soaps are soluble; the lead soap or plaster formed by boiling fat with litharge and water, is a soft insoluble mass; the magnesium and calcium soaps constitute the curdy scum, which is formed when soap is used with hard water.

Soap was known to the Romans, who probably made the necessary caustic alkali by boiling seaweed ashes with lime—they are said to have learned the method from the Gauls; it was an expensive luxury, however, and free caustic alkali and ammoniacal urine were generally used for cleaning.

The detergent action of soap is due to its hydrolysis by excess of water. Stearic acid and its congeners are very feeble acids, and although a strong solution of pure sodium stearate is neutral, it becomes alkaline on dilution owing to liberation of caustic soda. The soda combines with and loosens the greasy dirt, which is then enveloped in a lather by the insoluble acid salt, which is simultaneously set free (Chevreul, 1813). A second incidental advantage over caustic soda, is that it is impossible for the alkali to become concentrated, as on concentrating the solution soap is again formed; the hydrolytic action of the water is reversible, as in the case of ethyl acetate.

**49. Palmitic and Stearic Acids : Cetyl Alcohol.**—The fatty acids are set free by decomposing their alkali salts, the soaps, with dilute mineral acids. Stearic acid is readily obtained from mutton fat in this way. The soap is boiled with excess of dilute sulphuric acid, and the mixed oily acids which rise to the surface solidify to a cake on cooling. After thoroughly washing with water, the stearic acid is separated from the accompanying palmitic acid by fractional crystallisation from hot alcohol; it is less soluble than palmitic acid, and therefore tends to separate first.

The stearic acid is more readily separated by adding an alcoholic solution of magnesium acetate to the hot alcoholic solution of the mixed acids; the precipitate first thrown down consists of magnesium stearate (Heintz, 1852). "Stearin" candles are made of the mixture of stearic and palmitic acids, which is obtained by hydrolysing tallow with sulphuric acid at a high temperature (§ 127); the crude acids are purified by distillation with superheated steam, and are usually mixed with a certain proportion of solid paraffin (§ 79) to hinder crystallisation.

Palmitic acid is obtained from palm-oil, which consists principally of palmitin and olein (Heintz). The palmitic acid set free from the soap is separated from the freely soluble oleic acid (§ 133) by crystallisation from alcohol, the operation being repeated until the melting-point is constant (Fig. 12.) Sodium palmitate is also obtained by fusing oleic acid with caustic potash.

*Palmitic acid*,  $C_{15}H_{31}.COOH$  (Chevreul, 1813), crystallises from alcohol or ether in white needles, melts at  $62^{\circ}$ , and boils at  $356^{\circ}$ . *Stearic acid*,  $C_{17}H_{33}.COOH$  (Chevreul, 1826) =

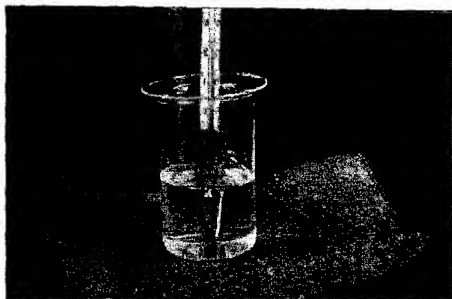


Fig. 12.—Determination of Melting-Point by Capillary Tube Method.\*

tallow), forms pearly plates, melts at  $69^{\circ}$ , and boils at about  $380^{\circ}$ . Both acids are decomposed when distilled under ordinary pressure, but they can be distilled unchanged under diminished pressure (§ 143) or in a current of superheated steam; the boiling points under 15 mm. pressure are  $215^{\circ}$  and  $232^{\circ}$  respectively.

Palmitic and stearic acids are inodorous and tasteless, but their alcoholic solutions redden litmus; they form derivatives which resemble chemically those of the lower fatty acids, and differ from them only quantitatively.

*Palmityl and stearyl chlorides* are stable solids, which are formed by the action of phosphorus pentachloride on the acids. *Palmitic anhydride* is a white crystalline solid melting at  $56^{\circ}$ , which is formed by heating palmitic acid with acetic anhydride at  $150^{\circ}$ . *Stearic anhydride* is a similar substance, melting at  $77^{\circ}$ . *Ethyl stearate*, which is made by passing hydrogen chloride into an alcoholic solution of the acid, melts at  $33^{\circ}$ .

\* See Laboratory Notes.

The natural waxes are ethereal salts of the fatty acids with alcohols of the ethyl series. Spermaceti, the wax which crystallises from sperm oil, is *cetyl palmitate*,  $C_{16}H_{33}O.OC_{16}H_{31}$ .

The cetyl alcohol can be isolated by hydrolysing the wax with boiling alcoholic potash, and precipitating the palmitic acid with barium chloride. The barium palmitate is filtered off, and the cetyl alcohol separates on concentrating the solution.

*Cetyl alcohol*,  $C_{16}H_{33}.OH$ . (Chevreul, 1823), is a white, crystalline, wax-like substance, which melts at  $49^{\circ}$ , and boils at  $344^{\circ}$ , or at  $189^{\circ}$  under a pressure of 15 mm.; it is inodorous and tasteless.

When heated with soda-lime it is oxidised to the alkali palmitate, hydrogen being evolved; conversely, palmitic acid is reduced to cetyl alcohol when warmed with zinc dust and acetic acid. *Stearyl alcohol*,  $C_{18}H_{37}.OH$ , a crystalline solid melting at  $59^{\circ}$ , is made from stearic acid in the same way. These alcohols form *chlorides, iodides, esters*, etc., in the same way as the liquid alcohols.

Beeswax consists of *myricyl palmitate*,  $C_{16}H_{31}O.OC_{30}H_{61}$ , and *ceryl cerotate*,  $C_{27}H_{55}O.OC_{27}H_{55}$ .

#### 50. Homologous Series: the Aliphatic Alcohols and Acids.—

The alcohols and acids, of which acetic acid and ethyl alcohol are the types, form two parallel series, the members of which are strikingly similar in properties; the alcohols resemble ethyl alcohol in forming esters, ethers, etc., and the acids resemble acetic acid.

The lowest members of these series are liquids which have marked and pleasant odours, and are freely soluble in water. As the series are ascended, the solubilities diminish, and the liquids become more viscous and oily; at the same time their odours become unpleasant. The ten-carbon alcohol and acid are practically insoluble in water, but have only faint odours. The sixteen-carbon compounds, cetyl alcohol and palmitic acid, are wax-like, crystalline substances, which are quite insoluble in water, and odourless. The same gradation of properties is noticeable in the ethereal salts, although the odour of these, however powerful, is never actually unpleasant.

The acids of the acetic series are termed the fatty or aliphatic acids, from the origin of the higher members, and the whole group of compounds, from its relationship to the acids, is known as the fatty or aliphatic\* group of compounds.

With respect to composition a remarkable relationship exists amongst the individual members of the several series.

\*  $\alpha\lambda\epsilon\iota\phi\alpha\rho$  = oil.

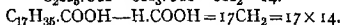
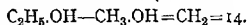
The alcohols and acids, as organic hydroxides, bear a general analogy to the alkali hydroxides and inorganic hydroxyacids; and this analogy extends to the graduated increase in molecular weight, and concurrent alteration in physical properties. But instead of the molecular increment being merely approximately regular, as in the inorganic series, it is perfectly regular and constant.

THE ALIPHATIC ALCOHOLS AND ACIDS (§ 81).

Methyl alcohol (65°)  $\text{CH}_3\text{OH} \longleftrightarrow$  Formic acid (101°)  $\text{CHO.OH}$   
 Ethyl alcohol (78°)  $\text{C}_2\text{H}_5\text{OH} \longleftrightarrow$  Acetic acid (118°)  $\text{C}_2\text{H}_3\text{O.OH}$   
 Propyl alcohol (97°)  $\text{C}_3\text{H}_7\text{OH} \longleftrightarrow$  Propionic acid (141°)  $\text{C}_3\text{H}_7\text{O.OH}$   
 Butyl alcohol (117°)  $\text{C}_4\text{H}_9\text{OH} \longleftrightarrow$  Butyric acid (162°)  $\text{C}_4\text{H}_7\text{O.OH}$   
 Amyl alcohol (138°)  $\text{C}_5\text{H}_{11}\text{OH} \longleftrightarrow$  Valeric acid (186°)  $\text{C}_5\text{H}_9\text{O.OH}$

Cetyl alcohol (344°)  $\text{C}_{16}\text{H}_{33}\text{OH} \longleftrightarrow$  Palmitic acid (356°)  $\text{C}_{16}\text{H}_{31}\text{O.OH}$   
 Stearyl alcohol (—)  $\text{C}_{18}\text{H}_{37}\text{OH} \longleftrightarrow$  Stearic acid (380°)  $\text{C}_{18}\text{H}_{35}\text{O.OH}$

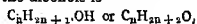
The members of these series differ in formulæ uniformly by  $\text{CH}_2$ , or a multiple of this group, and in molecular weight by 14, or a multiple of this number (Schiel, Dumas, 1842)—



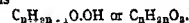
This relationship, which in such exact form is unknown amongst inorganic compounds, is termed homology (Gerhardt, 1844; *ὁμολογος*, agreeing). The series are termed homologous series, and their members are known as homologous compounds, or homologues. Methyl alcohol is thus the lower homologue of ethyl and cetyl alcohols, and stearic acid the higher homologue of formic and valeric acids.

It is obvious that homology obtains in all the series of compounds. Methyl chloride, for example, is homologous with ethyl and propyl chlorides; propyl hydrogen sulphate is homologous with the other alkyl sulphates, and stearic anhydride is homologous with acetic anhydride.

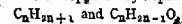
Homologous compounds may be represented by general formulae. The general formula of the alcohols is



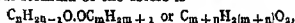
and that of the acids is



The alkyl and acyl radicals are respectively represented by the formulæ



so that the general formula of the esters is



which is identical with the general formula of the acids (cf. § 51).



**51. Isomerism and Metamerism.**—Many of the oxides and hydroxides are related in another manner, which again is peculiar to organic compounds. It often happens in the varied combinations of the homologous radicals that compounds are formed, which although quite distinct from one another, have the same composition and formula (cf. § 50). Thus :

Methyl propionate . . .	$C_2H_5.CO.OCH_3$ ,
Ethyl acetate . . . .	$CH_3.CO.OC_2H_5$ and
Propyl formate . . . .	$H.CO.OC_3H_7$

have the same empirical formula,  $C_3H_6O$ . Methyl formate and acetic acid, and alcohol and methyl ether, form similar pairs.

Compounds such as these, which have the same composition and formulæ, but different properties, are termed isomeric compounds, or isomerides (Berzelius, 1838; *isos*=equal, *meros*=a part), and the relationship between them is known as isomerism. There are many forms of isomerism amongst organic compounds. This particular form is sometimes known as metamerism; the term, however, is now rarely used.

**52. Synopsis.**—The fats, waxes and soaps are ethereal or metallic salts of complex acids of the acetic series, and on this account the acetic and related series are collectively termed the fatty or aliphatic group. The members of the various series differ in composition by regular atomic increments, and are hence termed homologues. Many of them are identical in composition but different in properties, and are hence termed isomerides.

## SECTION II

### SYNTHESIS AND MOLECULAR STRUCTURE

#### CHAPTER X

##### ACETAMIDE AND ETHYLAMINE

**53. Acetamide.**—As ethyl acetate is hydrolysed to its proximate constituents by alkalis, in the same way as a metallic salt, one would expect ammonia to have the same action. But instead of ammonium acetate, a dehydrated product termed acetamide is obtained; the reaction was first observed with ethyl oxalate (Liebig, 1834).

When ethyl acetate is added to an equal volume of concentrated ammonia, the liquids do not at first mix, but they become homogeneous if occasionally shaken; in winter the mixture should be kept in a warm place, but it is unnecessary to heat it in a sealed tube.

On distilling the product a day or two later, the excess of ammonia is first expelled, and then a solution of ammonia in dilute alcohol passes over, followed by water alone. Finally the thermometer rises rapidly to over  $200^{\circ}$ , and an oily liquid distils, which soon crystallises to a white solid; it is best to remove the condenser at this stage, and receive the distillate in a test tube cooled with wet filter paper.

The crude product usually melts at about  $60^{\circ}$ , but by removing the accompanying liquid by draining the warm product quickly at the filter-pump, the melting point is raised  $10^{\circ}$  or more, and on re-melting, and repeating this fractional crystallisation it eventually becomes constant.

*Acetamide*,  $\text{CH}_3\text{CO.NH}_2$  (Dumas, 1847), is a colourless, crystalline substance, which melts at  $82^{\circ}$ , boils at  $222^{\circ}$ , and sublimes slowly in long needles when kept at a temperature slightly below its melting point; it is freely soluble in water and alcohol, and very hygroscopic. The crude product smells like mice, but this is due to an impurity, for after washing

with dry ether, or recrystallising from hot chloroform, it becomes practically odourless.

**54. Detection and Estimation of Nitrogen.**—Acetamide contains nitrogen, as well as carbon and hydrogen. There are two methods of detecting nitrogen in an organic compound. In the first method, the substance is mixed with powdered soda-lime, and heated to redness in a test-tube; if nitrogen is present, ammonia is evolved, and can be recognized by the usual tests. This test fails with certain substances, and if it gives a negative result (but not otherwise) must be supplemented by a second test, which is almost universally applicable.

A small portion of the substance is heated with excess of sodium in a small test-tube, and after the first action is over the mass is heated to full redness for at least half a minute; this heating is essential. Under these conditions, the nitrogen is converted into sodium cyanide, which can be identified by conversion into Prussian blue (Lassaigne, 1843; § 202).

The test-tube is broken with water while hot; the solution of cyanide is filtered from carbon, and warmed with ferrous and ferric solutions and excess of alkali; on then acidifying with hydrochloric acid, Prussian blue is precipitated.

The best method of estimating nitrogen in an organic compound consists in burning the substance with copper oxide in a combustion tube, and measuring the liberated nitrogen (Dumas, 1831). It is termed the absolute method. The substance is mixed with part of the copper oxide, instead of resting in a boat as in the carbon combustion, and carbon dioxide is passed through the tube before and after the combustion, to expel the air and nitrogen. The gases, after passing over red-hot copper gauze, to decompose oxides of nitrogen, are collected over mercury, in a graduated tube, which contains strong caustic potash solution, to absorb the carbon dioxide (Fig. 13). The weight of nitrogen is then calculated from the volume of gas remaining.

The nitrogen in physiological and agricultural products can usually be estimated with sufficient accuracy by conversion into ammonia (Kjeldahl, 1883). The substance is heated with concentrated sulphuric acid on a sand-bath until the carbon is completely oxidised, and the solution is clear and nearly colourless; a little potassium permanganate or mercuric oxide is sometimes added towards the end of the operation to complete the oxidation. The nitrogen is thus converted into ammonium sulphate.

Excess of caustic soda solution is now cautiously added, and the ammonia is distilled off into a known amount of standard sulphuric acid, and determined volumetrically. The process is not used in pure chemical investigations, as many substances fail to yield the whole of their nitrogen as ammonia, when treated in this manner. An older method, in which the substance is distilled with soda-lime, is open to the same objection.

In a nitrogen combustion of acetamide.

0.1096 gram gave 22.6 cc. of moist nitrogen, at 20° and 769 mm.

The weight of this volume of gas is

$$0.0262 \text{ gram,*}$$

and the percentage of nitrogen

$$(0.0262/0.1096) \times 100 = 23.9.$$

In the estimation of carbon and hydrogen in nitrogenous substances a long roll of red-hot copper or silver gauze is placed after the copper oxide,

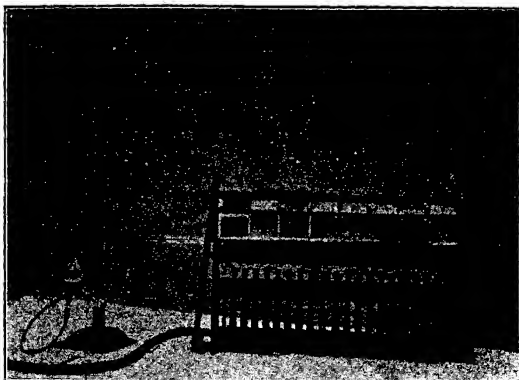


Fig. 13.—Estimation of Nitrogen by Combustion with Copper Oxide.

The carbon dioxide is generated by heating sodium hydrogen carbonate or magnesite. The mercury at the bottom of the nitrometer or measuring-tube prevents the passage of the potash into the combustion tube.

to decompose any oxides of nitrogen that may be formed; these would otherwise be absorbed in the sulphuric acid or potash of the absorption bulbs, and spoil the analysis.

In a carbon combustion of acetamide

0.1937 gram gave 0.2884 gram  $\text{CO}_2$  and 0.1492 gram  $\text{H}_2\text{O}$ ;

C = 40.61, H = 8.56 per cent.

The empirical formula  $\text{C}_2\text{H}_5\text{NO}$  requires

C = 40.68, H = 8.48, N = 23.73, O = 27.10.

**55. Relation of Acetamide to Acetic Acid and Ammonia; its Hydrolysis.**—The empirical formula of acetamide,  $\text{C}_2\text{H}_5\text{NO}$ , is also the molecular formula indicated by the vapour density. The formation of acetamide from ethyl acetate is therefore represented by the following equilibrium equation.

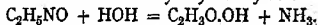


When acetamide is boiled with caustic soda solution, it

\*  $22.6 \times (752/760) \times (273/293) \times 0.001256$  (0.001256 = weight of 1 cc. of nitrogen at 0° and 760 mm.; pressure of water vapour at 20° = 17 mm.)

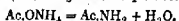
gives off the whole of its nitrogen as ammonia, and on distilling the residue with dilute sulphuric acid, acetic acid passes over. The same decomposition is effected by boiling with dilute sulphuric acid; acetic acid now passes over, and ammonium sulphate remains in the residue.

Acetamide is thus readily hydrolysed.



As it is both made from and convertible into acetic acid, acetamide must contain the acetyl radical, so that its rational formula is  $\text{C}_2\text{H}_5\text{O.NH}_2$  or  $\text{Ac.NH}_2$ . The amide is therefore derived from the acid by the exchange of hydroxyl for amidogen, and the ammonia in its formation behaves as nitrogen hydride, and not as ammonium hydroxide.

This rational formula of acetamide is confirmed by other modes of formation. The amide is generated by the interaction of acetyl chloride with ammonium carbonate, or even with aqueous ammonia (Gerhardt, 1853). It is also formed by distilling ammonium acetate, or heating it in a sealed tube at  $155^\circ$  (Kundig, 1858). The yield, however, is poor in both cases.

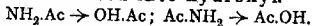


The constitution of acetamide accords with the neutral character of the substance. It behaves both as a feeble acid and as a feeble base. On warming its aqueous solution with yellow mercuric oxide, the oxide dissolves; and on cooling the solution, a crystalline *mercury acetamide*,  $\text{Hg}(\text{NHAc})_2$ , separates. On the other hand, on passing dry hydrogen chloride into an alcohol-ether solution of the amide, unstable crystalline *acetamide hydrochloride*,  $\text{AcNH}_2\text{HCl}$ , is precipitated.

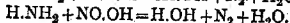
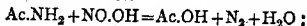
Acetamide may thus be regarded as ammonia, in which one of the hydrogen atoms is replaced by acetyl—



and this view is borne out by its behaviour with nitrous acid; the nitrogen is eliminated in the free state, and the amidogen is converted into hydroxyl.



The action is exactly parallel to the preparation of nitrogen by heating ammonium nitrite.

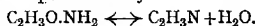


On adding dilute sulphuric acid drop by drop to a solution containing equimolecular quantities of acetamide and sodium nitrite, the nitrous acid which is liberated interacts with the amide just as it does with ammonia. The acetamide nitrite which is probably formed, is much less stable even than ammonium nitrite, and decomposes rapidly on warming, giving nitrogen and acetic acid; when excess of sulphuric acid has been added, the acetic acid may be distilled off.

**56. Acetonitrile.**—Acetamide can be further dehydrated. When roughly mixed with twice its bulk of phosphorus pentoxide, and gently heated in a small flask or test tube, which is connected with a condenser, a colourless liquid distils, whilst phosphoric acid remains behind.

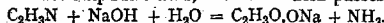
The distillate contains acetic acid, which is liberated from some of the acetamide by the phosphoric acid which is formed from the pentoxide; this is eliminated by boiling in a reflux apparatus with powdered, fused potassium carbonate, and on redistillation the liquid now boils at a constant temperature. Acetonitrile can be obtained directly from ammonium acetate, but a much larger quantity of the pentoxide is necessary, and much more acetic acid is formed.

*Acetonitrile*,  $\text{CH}_3\text{CN}$  (Dumas, 1847), is a colourless, volatile liquid, which boils at  $82^\circ$ . It has a peculiar, unpleasant, ethereal odour reminiscent of dilute prussic acid, and burns with a characteristic purple-mantled flame. The empirical formula is  $\text{C}_2\text{H}_3\text{N}$ , and this is also the molecular formula indicated by the vapour density.



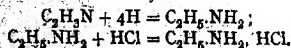
The nitrile thus bears the same relation to acetamide as the latter bears to ammonium acetate; it can be reconverted into the amide by heating with water in a sealed tube at  $180^\circ$ , or warming with an alkaline solution of hydrogen peroxide.

Like acetamide, acetonitrile is hydrolysed by alkalis and acids to acetic acid and ammonia. The liquid is simply boiled with caustic soda solution in a reflux apparatus, until ammonia ceases to be evolved, and on distilling the residual liquid with excess of dilute sulphuric acid, the acetic acid passes over.



**57. Ethylamine.**—Acetonitrile not only takes up water, but readily combines with the equivalent amount of hydrogen. If the nitrile be dissolved in dilute sulphuric acid, and zinc added in small quantities from time to time, its odour eventually disappears. On distilling the product with excess of caustic soda, and collecting the distillate in a little water, an alkaline solution is obtained which is strikingly like ammonia in odour and general actions.

But the hydrochloride which is obtained, when the liquid is neutralised and evaporated, is soluble in alcohol; and the gas which is liberated on heating this hydrochloride with lime is inflammable; it is termed ethylamine.



A better yield of ethylamine is obtained by reducing the nitrile with metallic sodium in boiling alcoholic solution (Ladenburg, 1886). The operation is carried out in a reflux apparatus supplied with condensing water at about 50°, so that most of the alcohol returns, whilst the ethylamine vapour passes over. It is collected in dilute hydrochloric acid, best in a Volhard trap (Fig. 18, § 114).

The ethylamine hydrochloride made by reducing acetonitrile (Mendius, 1862) is accompanied by ammonium chloride, from which it is separated by extracting the evaporated residue with a mixture of absolute alcohol and ether, in which the ammonium chloride is insoluble. The solution is filtered, and the solvent distilled off in a water bath.

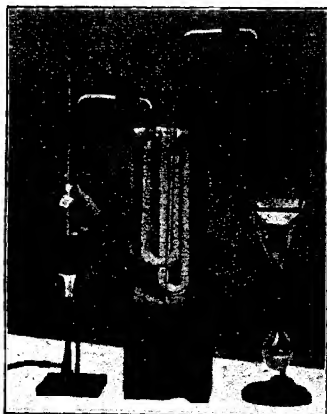
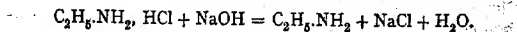


Fig. 14.—Preparation of Pure Ethylamine.

Free ethylamine is prepared by heating the hydrochloride with lime or concentrated caustic soda, as in the preparation of ammonia, and after drying with warmed quicklime is condensed in a freezing mixture (Fig. 14); it cannot be dried with calcium chloride, as like ammonia it forms a compound with this substance.



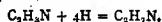
*Ethylamine*,  $\text{C}_2\text{H}_5\text{NH}_2$  (Wurtz, 1848), is a colourless volatile liquid, which boils at 18°, and has a specific gravity of 0.699 at 8°; its odour is strongly ammoniacal, but when diluted

recalls that of stale fish. Both the liquid and the vapour are very soluble in water, and the solution has most of the properties of aqueous ammonia; it fumes with hydrochloric acid, is strongly alkaline, absorbs carbon dioxide freely, and precipitates metallic hydroxides.

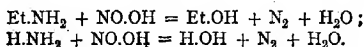
Ethylamine vapour is readily distinguished from ammonia, as it is heavier than air, and inflammable, and can be condensed to a liquid at ordinary temperatures; moreover the products of its combustion contain carbon dioxide.

*Ethylamine hydrochloride*,  $C_2H_5N, HCl$ , is a feathery crystalline substance, which is distinguished from ammonium chloride by its deliquescence and solubility in alcohol.

The presence of nitrogen in ethylamine is proved by the formation of sodium cyanide, when its vapour is passed over red-hot sodium. The empirical and molecular formula deduced from the analysis and vapour density is  $C_2H_7N$ . As no oxygen is present, the substance is formed by direct addition of hydrogen to acetonitrile.



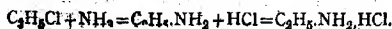
**58. Relation of Ethylamine to Alcohol and Ammonia: Distinction from Acetamide.**—From its mode of preparation it is evident that, unlike acetamide and acetonitrile, ethylamine is not hydrolysed by alkalies and acids. On the other hand, it resembles acetamide in its action with nitrous acid, by which it is converted into alcohol, the amidoglycer being converted into hydroxyl (Hofmann, 1849).



When a solution of equimolecular quantities of ethylamine hydrochloride and sodium nitrite is heated, the ethylamine nitrite, which is formed transiently, is at once decomposed; the whole of the nitrogen is evolved in the free state, and on distilling the solution alcohol passes over.

Ethylamine thus bears the same relation to alcohol as acetamide bears to acetic acid, and is represented by a rational formula analogous to that of acetamide. It may be regarded as ammonia, in which a hydrogen atom is replaced by ethyl.

This is confirmed by its preparation from ammonia and the ethyl haloids (Hofmann, 1849); when ethyl chloride is heated in a closed vessel with excess of alcoholic ammonia, ethylamine hydrochloride is formed, together with ammonium chloride and other products (§ 212).





The liquid is concentrated and cooled, to separate the ammonium chloride, and on further evaporation, crude ethylamine hydrochloride crystallises out; it may be separated from ammonium chloride by means of alcohol-ether as above, but there are also more complex amines present, separation from which is very tedious.\* Ethylamine may also be made in other ways; it was first prepared from ethyl cyanate.

The difference between ethylamine and acetamide is of the same order as between alcohol and acetic acid, or ether and ethyl acetate. Ethylamine is a stronger base than ammonia, because of the influence of the positive ethyl radical, and acetamide is a weaker base, because of the influence of the negative acetyl radical. For the same reason the acetyl derivatives are more easily hydrolysed than the ethyl derivatives; ethyl acetate and acetamide are both easily decomposed by caustic alkalies, whereas ether and ethylamine are unaffected by these agents (compare § 40).

The introduction of the ethyl group into ammonia increases, whilst the introduction of the acetyl group decreases the stability. The difference is ultimately resolvable into the difference between oxygen and hydrogen. The acetyl radical contains an oxygen atom in place of two of the hydrogen atoms of the ethyl radical. Oxygen is electronegative or acidic, hydrogen electropositive or basic; hence the substitution of oxygen for hydrogen converts the feebly basic ethyl into the strongly acid acetyl radical. Alcohol is more basic, and acetic acid more acid than water. Ethylamine is more basic, but acetamide less basic than ammonia.

$C_2H_5.OH$ feebly basic	$H.OH$ neutral	$C_2H_5.O.OH$ acid
$C_2H_5.NH_2$ strong base not hydrolysable	$H.NH_2$ base	$C_2H_5.O.NH_2$ neutral hydrolysable
$C_2H_5.OEt$ hydrolysed with difficulty		$C_2H_5.O.OEt$ easily hydrolysed

53. **Determination of Molecular Weight by the Platinum Method.**—Ethylamine salts, like ammonium salts, form numerous metallic compounds. *Ethylamine platinichloride*,  $(NH_2Et, HCl)_2$ ,  $PtCl_4$ , an orange, crystalline substance, resembling ammonium platinichloride, is precipitated when platinum chloride is added to an alcoholic or concentrated aqueous solution of ethylamine hydrochloride. The *aurichloride* and *mercurichloride* are similar compounds.

The molecular weight of a basic ammonia derivative like ethylamine, can be determined by analysis of its platinichloride, in the same way as the molecular weight of an acid is determined by analysis of its silver salt. The dry platinichloride is heated to redness in a crucible; the carbon, hydrogen, nitrogen and chlorine are eliminated in volatile form, and metallic platinum is left. Ammonium platinichloride is decomposed in the same way.

\* The amines, of which ethylamine is the type, are more fully discussed in Chapter xxxix.

In an analysis of dry ethylamine platinichloride  
0.3706 gram gave 0.1437 gram Pt,  
from which the

percentage of platinum is 38.78

As the empirical formula of ethylamine is  $C_2H_7N$ , the possible molecular formulæ are  $C_2H_7N$ ,  $C_4H_{14}N_2$ ,  $C_6H_{21}N_3$ , etc. Further, as ethylamine forms only one hydrochloride, whatever the proportion in which it is mixed with the acid, it is a monacid base like ammonia, and its platinichloride must be of the type  $(X.HCl)_3.PtCl_4$ .

The possible formulæ of ethylamine platinichloride, and the corresponding percentages of platinum, are therefore

Formula.	Percentage of Platinum.
$(C_2H_5N.HCl)_3.PtCl_4$	38.69
$(C_4H_{14}N_2.HCl)_3.PtCl_4$	32.83
etc.	etc.

The analysis, although slightly inaccurate, shows that the first formula is correct, and that the molecular formula of ethylamine is



**60. Synopsis.**—The ethyl and acetyl radicals form nitrogen compounds, which bear the same relation to ammonia as the alcohols and acids to water. The alkyl derivative, ethylamine, is a powerful base, resembling ammonia, and not hydrolysable, whilst the acidyl derivative, acetamide, is a neutral substance, which is easily hydrolysable to acetic acid and ammonia. Both compounds are converted into the corresponding hydroxides by nitrous acid, and are genetically connected by an intermediate compound, acetoneitrile.



## CHAPTER XI

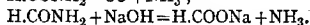
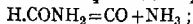
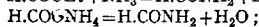
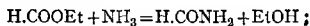
### THE CYANIDE SYNTHESIS

**61. Formamide : Formonitrile or Hydrogen Cyanide.**—Acetamide, acetonitrile and ethylamine are types of three great classes of compounds: the amides, the nitriles and the amines. There is an amide corresponding with each acid, and an amine corresponding with each alcohol; and each pair are connected by a corresponding nitrile.

The simplest amide, formamide, is made by the action of ammonia on ethyl formate, or by heating ammonium formate in a sealed tube at  $230^{\circ}$ .

The product is fractionated under reduced pressure, as formamide is less stable than acetamide; it is obtained as an oily liquid, which when quite dry can be frozen to a crystalline solid.

*Formamide*,  $\text{H.CONH}_2$  (Hofmann, 1863), melts at  $1^{\circ}$ , and boils at  $192^{\circ}$ , at the same time partially decomposing into carbon monoxide and ammonia (compare Formic acid). Like acetamide, it is hydrolysed to ammonia and the acid when boiled with caustic alkalies.



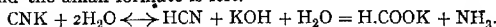
When dry formamide is warmed with phosphorus pentoxide, it is decomposed into water and formonitrile, but the yield is far poorer than with acetonitrile, because most of the amide is hydrolysed. The product is dried by simple rectification over phosphorus pentoxide.

Formonitrile is identical with hydrogen cyanide or prussic acid, and is most readily prepared from potassium cyanide (§ 201).

A cold mixture of sulphuric acid with an equal volume of water is allowed to drop slowly on lumps of pure potassium cyanide; there is a brisk action, and hydrogen cyanide vapour is evolved; it is dried by passing over warm calcium chloride, and condensed in an ice-cooled U-tube (Fig. 14, § 57).

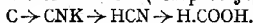
*Formonitrile* or *hydrogen cyanide*, HCN (Scheele, 1782), is a very mobile and volatile liquid, which boils at  $26^{\circ}$ , and freezes at  $-15^{\circ}$ ; like acetonitrile it burns with a purple-tinged flame. Its odour is harsh and unpleasant, and leaves an unpleasant after-taste; both the liquid and vapour are excessively poisonous, and the anhydrous product should not be made without special reason. The best antidote to inhalation of the vapour is dilute ammonia gas.

**62. Synthesis of Formic Acid and Methyl Alcohol from Carbon.**—Hydrocyanic acid, being identical with formonitrile, is hydrolysed by alkalis to the alkali formate and ammonia. The hydrolysis is effected by boiling an aqueous solution of potassium cyanide in a reflux apparatus, preferably with excess of caustic alkali. Hydrogen cyanide is so feebly acid, that its alkali salts in solution are partially dissociated into the acid and free caustic alkali. The hydrolysis is therefore parallel to that of acetonitrile; ammonia is evolved in abundance, and the alkali formate is left.



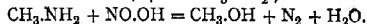
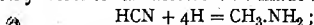
The entire conversion requires some time, and the cyanide left after boiling for an hour is conveniently eliminated by gently distilling the product with excess of dilute sulphuric acid; the unchanged hydrogen cyanide is quickly expelled, and the distillate eventually ceases to precipitate silver nitrate. The formic acid may then be distilled.

As potassium cyanide can be made from its elements, the conversion of hydrogen cyanide into formic acid affords an additional synthesis of this acid (compare § 44).



Just as acetonitrile can be reduced to ethylamine, which is convertible into ethyl alcohol, formonitrile is reducible to an analogous compound, methylamine, which is convertible into methyl alcohol.

Methyl alcohol can therefore be made from its elements.



The reduction is effected by zinc and dilute sulphuric acid, in the same way as with acetonitrile (the sodium method cannot be used, as sodium cyanide is formed). When hydrogen ceases to be absorbed by the liquid, the product is made alkaline and distilled; the methylamine passes over as a highly alkaline, ammoniacal vapour, which resembles ethylamine in all essentials.\* On neutralising the amine with hydrochloric acid, and

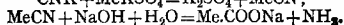
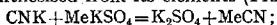
\* This is not the best way of preparing methylamine and its homologues; for other methods and a fuller discussion of the amines see Chapter xxx.

warming it with sodium nitrite solution, nitrogen is evolved, and methyl alcohol is formed.

**63. Methyl Cyanide : Synthesis of Acetic Acid and Ethyl Alcohol : Third Rational Formulae.**—The identity of hydrogen cyanide with formonitrile suggests that acetonitrile is identical with methyl cyanide, and that acetic acid is consequently a methyl derivative (Frankland, 1847).

When a mixture of methyl potassium sulphate with powdered potassium cyanide is heated at about  $200^{\circ}$ , a colourless liquid distils, which contains a considerable quantity of methyl alcohol from decomposition of the alkyl sulphate. On removing the alcohol by repeated treatment with phosphorous pentoxide, which also eliminates a malodorous impurity (methyl isocyanide, § 203), a liquid is obtained having the composition of methyl cyanide.

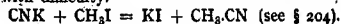
*Methyl cyanide*,  $\text{CH}_3\text{.CN}$ , is a liquid which boils at  $82^{\circ}$ , and is in every respect identical with acetonitrile. When hydrolysed with alkali it is converted into ammonia and the alkali acetate; acetic acid is therefore a methyl compound, and can be synthesised from its elements (Frankland, 1847).



Methyl cyanide does not give the ordinary reactions for cyanides, such as the Prussian blue test. The cyanogen radical is so firmly united with the methyl that it is impossible to separate it as such; when the compound is decomposed, it is the cyanogen itself which changes, and it is this fact which makes the above synthesis possible.

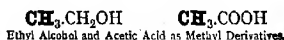
For the verification of the synthesis of acetic acid, it is unnecessary to isolate the methyl cyanide. The crude distillate is boiled with concentrated caustic soda solution until ammonia ceases to be evolved. It is then acidified with dilute sulphuric acid, and boiled, still in the reflux apparatus, with a little mercuric oxide, to oxidise some formic acid which is produced as a bye-product. On distilling the acid liquid, dilute acetic acid passes over, and may be identified qualitatively, and by analysis of its silver salt.

An alcoholic solution of methyl cyanide suitable for the synthesis may be prepared from methyl iodide (Buckton and Hofmann, 1856). The iodide is poured down the condenser of a reflux apparatus, containing pure potassium cyanide covered with 80 per cent. alcohol (potassium cyanide is nearly insoluble in absolute alcohol). There is soon a brisk action, which is completed by boiling on a water-bath for an hour. On reversing the condenser, and distilling the product to dryness, acetonitrile and alcohol pass over together as a mixture of constant boiling-point; they can only be separated with difficulty.

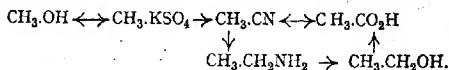


As methyl cyanide is identical with acetonitrile, it is converted by reducing agents into ethylamine; and as ethylamine is transformed into alcohol by nitrous acid, it follows that ethyl alcohol is also a methyl derivative, and can be synthesised from its elements.

As a result of the cyanide synthesis, a third pair of rational formulæ must be given to ethyl alcohol and acetic acid—



These formulæ emphasise the relation between ethyl alcohol and methyl alcohol, and embody the fact that the methyl group passes intact through this intricate set of changes.



**64. Synthesis of the Higher Alcohols and Acids: the Higher Amides and Nitriles.**—The conversion of methyl alcohol into acetic acid is a typical instance of Organic Synthesis, or building up an organic radical from others containing fewer carbon atoms. The principle thus established can be extended indefinitely, as the nitriles made by dehydrating the higher amides are in every case identical with the cyanides of the next lower alkyl radicals.

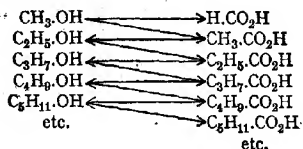
The amides are neutral, crystalline substances, which are prepared in the same way as acetamide, and resemble it in all essentials; when boiled with alkali, they are resolved hydrolytically into their proximate constituents, namely ammonia and the corresponding acid. *Propionamide*,  $\text{C}_2\text{H}_5\cdot\text{CONH}_2$ , melts at  $79^\circ$ , and boils at  $213^\circ$ . *Butyramide*,  $\text{C}_3\text{H}_7\cdot\text{CONH}_2$ , melts at  $115^\circ$ , and boils at  $216^\circ$ . *Palmitamide*,  $\text{C}_{15}\text{H}_{31}\cdot\text{CONH}_2$ , melts at  $107^\circ$ , and *stearamide*,  $\text{C}_{17}\text{H}_{35}\cdot\text{CONH}_2$ , at  $109^\circ$ .

On distillation with phosphorus pentoxide, or in some cases with less energetic agents, the amides are dehydrated to nitriles, homologous with acetonitrile. As these also are identical with the alkyl cyanides, they can be made synthetically from the next lower alcohols, and are resolved hydrolytically into ammonia and the corresponding acid, when boiled with alkali.

*Propionitrile* or *ethyl cyanide*,  $\text{C}_2\text{H}_5\cdot\text{CN}$ , boils at  $98^\circ$ . *Butyronitrile* or *propyl cyanide*,  $\text{C}_3\text{H}_7\cdot\text{CN}$ , boils at  $118^\circ$ . *Palmitonitrile* or *pentadecyl cyanide*,  $\text{C}_{15}\text{H}_{31}\cdot\text{CN}$ , and *stearonitrile* or *heptadecyl cyanide*,  $\text{C}_{17}\text{H}_{35}\cdot\text{CN}$ , are crystalline solids which melt at  $29^\circ$  and  $41^\circ$  respectively; they can be distilled unchanged under reduced pressure.

Ethyl alcohol can thus be converted into ethyl cyanide, propionic acid and propyl alcohol; propyl alcohol can be converted into propyl cyanide, butyric acid and butyl alcohol.

and so on almost indefinitely. By this and other methods, all the compounds which we have thus far considered have been prepared synthetically from their elements. The aliphatic acids and alcohols, up to the nine-carbon members, may be made from methyl alcohol by the cyanide synthesis (Lieben and Rossi, 1871-1877).



Above the two-carbon compounds the alcohols are obtained from the synthesised acids by reducing the aldehydes (§ 86), propylamine and its higher homologues being converted by nitrous acid, not simply into the corresponding alcohols, but partly into isomeric compounds; but the synthesis is equally valid.

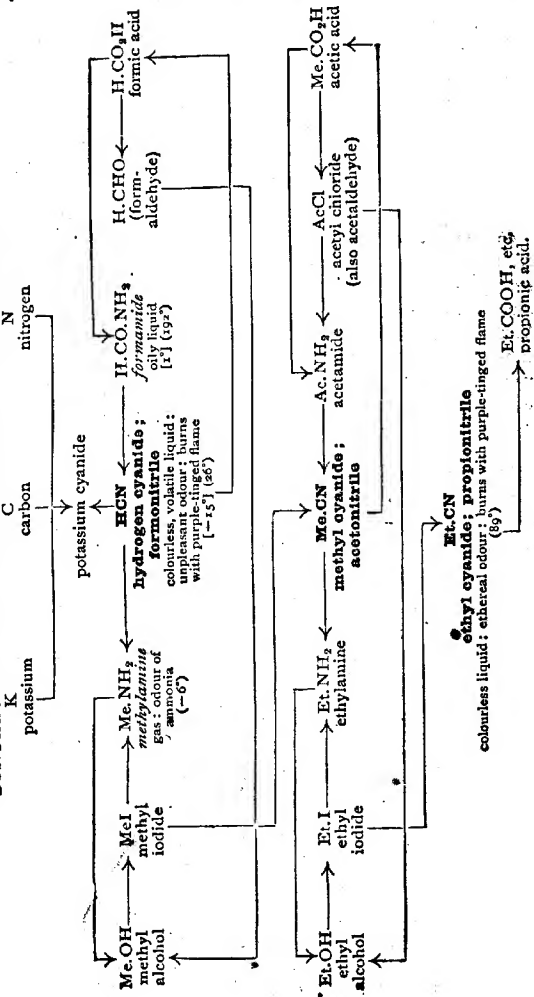
It is difficult to carry out work as extensive as this. The yield of product in Organic operations rarely approaches that indicated by the equations; not only is loss inevitable in boiling, distillation, crystallisation, etc., but in many cases the action is diverted into secondary channels by comparatively slight alterations in conditions. In the preparation of the cyanides from the alcohols, for example, considerable quantities of isomeric impurities are sometimes formed.

The actual conversion of the substance at one end of a chain into that at the other end is not essential, provided that each link is established. It is much easier in the above chain of syntheses to make ethyl alcohol from sugar than from methyl alcohol; all that is necessary for synthetic purposes is to prepare enough ethyl alcohol from methyl alcohol, or even from acetic acid, to establish its identity. Once this is proved, the more accessible product may be used as a fresh starting-point. In this way, by testing the links separately, many chains of synthetic relations have been established, which might not otherwise have been realised. The sugars afford a notable instance of this (§ 187).

**65. Synopsis.**—Formonitrile is identical with hydrogen cyanide, and its homologues are identical with the alkyl cyanides. By means of these the lower alcohols and acids and their derivatives can be converted into their higher homologues, and all can be synthesised from the elements.



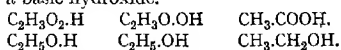
## SYNTHESIS OF THE ALIPHATIC ALCOHOLS AND ACIDS.



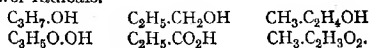
## CHAPTER XII

### MOLECULAR STRUCTURE

**66. Constitution or Structure : Valency.**—As a result of the cyanide synthesis, it follows that both alcohol and acetic acid are represented by no less than three rational formulæ, each of which indicates some chemical characteristic or relationship. Acetic acid, primarily an acid hydroxide, is also a methyl derivative, and in common with its homologues, a carboxyl compound. Alcohol is both a methyl and an ethyl derivative, as well as a basic hydroxide.

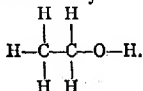


The more diverse the relations of a substance, the more numerous its formulæ become. From the cyanide synthesis alone it is obvious that the higher alcohols and acids contain all the lower radicals.



But the number of atoms in a molecule is fixed, and the molecules of a pure substance are all alike; hence the radicals represented in the various rational formulæ must be present together in each individual molecule (Gerhardt). The atoms must therefore be grouped within each molecule in an orderly manner, and their grouping must be such as to comprise all the smaller atomic groups or radicals.

The theory of structure (Kekulé, Couper, 1857), postulates that the atoms are held by mutual attraction, the direction of which may be symbolised by lines or "bonds" (Couper).



It is known from Inorganic Chemistry that there are very definite limits to the combining powers of the elements (Frankland, Kekulé, 1857). An atom of oxygen combines at the

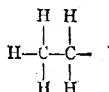
most with two other atoms, as in water; an atom of nitrogen with three, as in ammonia; and an atom of carbon with four, as in marsh gas. A hydrogen atom, on the other hand, does not combine with more than one atom of any kind, for no compound is known which is broken up by the simple removal of this element.

With the aid of these rules of valency, namely that hydrogen is univalent, oxygen bivalent, nitrogen trivalent and carbon quadrivalent, the internal molecular structure of a substance can be deduced from its chemical relations.

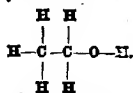
**87. Structure of the Aliphatic Alcohols and Acids.**—The active hydrogen of alcohol is removed when the oxygen is taken away, and this hydrogen atom is therefore linked to the oxygen atom.



As a hydrogen atom cannot serve as a link, the carbon atoms must be directly united, and the five hydrogen atoms attached to them.



The remaining carbon valency is satisfied by the unattached valency of the oxygen atom. The complete structure is therefore represented by the formula



Structural Formula of Ethyl Alcohol.

Similarly, the acetic acid molecule contains a hydroxyl group,



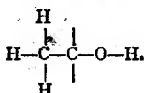
whilst as a methyl derivative it contains a methyl group,



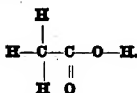
Further, as the acid can be made from and converted into alcohol and methyl cyanide (see below), its molecule contains the nucleus



These three conditions necessitate the arrangement

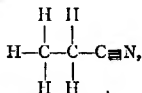


The two remaining valencies can only be satisfied by the second oxygen atom, and the structure of the acid is therefore represented by the formula



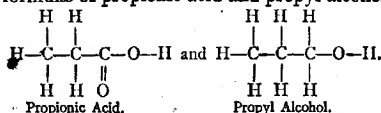
Structural Formula of Acetic Acid : the Carboxyl Radical.

The structure of the higher alcohols and acids also follows from the cyanide synthesis ; in the alkyl cyanides the nitrogen is detached by hydrolysis, and the cyanogen-carbon atom must therefore be linked to the alkyl. The structural formula of ethyl cyanide is thus



Propionitrile or Ethyl Cyanide.

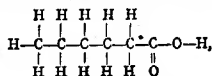
and the formulæ of propionic acid and propyl alcohol,



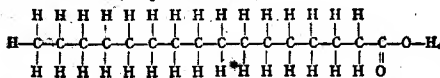
Propionic Acid.

Propyl Alcohol.

The formulæ of the higher alcohols and acids follow in the same way, an additional carbon atom being attached to the carbon chain at each step. Thus the structure of caproic acid is represented by the formula



and that of palmitic acid by a similar formula containing a chain of sixteen carbon atoms (for proof, see § 80)—



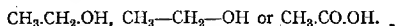
This capacity for forming chains is characteristic of the atoms of carbon and in part accounts for the very large number of carbon compounds.

**68. Structural and Constitutional Formulæ.**—Formulæ such as these, showing the arrangement of the atoms in a molecule, are termed structural formulæ. They epitomise the entire chemical behaviour of the substances they represent, and show at a glance their points of resemblance and difference.

The mobile hydrogen and hydroxyl of alcohol and acetic acid are marked. The synthesis of both compounds from methyl alcohol is accounted for. The mechanism of their oxidation and reduction is also apparent, the hydrogen of the non-methylic carbon being attacked, and the methyl group remaining unaltered. The greater activity of the carboxylic hydrogen is explained by the juxtaposition of the second oxygen atom.

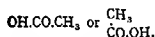
Given a structural formula, it is generally possible to form an accurate idea of the chemical behaviour of the substance.

The full graphic or structural formulæ are cumbersome, and are usually abbreviated into constitutional formulæ, such as

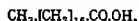


These convey the same information if the valencies are taken into account.

The actual position of the groups is immaterial provided that the proper order and linking are maintained. The formula of acetic acid may be also written as



In the case of long chain-formulæ containing a number of similar groups, it is convenient for the sake of brevity to place one of the groups in a square bracket, indicating the actual number by a suffix. Thus the constitutional formula of stearic acid may be written as



and that of spermaceti (§ 49) as



Constitutional formulæ are sometimes abbreviated into such forms as



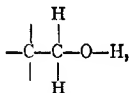
These are similar to the rational formulæ, but the dots represent linkages and are not mere marks of separation.

**69. Cause of Homology and Metamerism.**—Homology (§ 50) is due to the fixed valency of carbon. In methyl alcohol the valency of each atom is fully satisfied, and to introduce a second

carbon atom one of the hydrogen atoms must be removed—

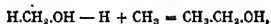


The carbon atom thus introduced has still three valencies disengaged—

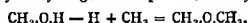


which require three more hydrogen atoms. The net result is the introduction of  $\text{CH}_2$ , the difference between  $\text{CH}_3$  and  $\text{H}$ .

If the methyl group replaces a methyl hydrogen atom, ethyl alcohol is produced—



whilst if the hydroxylic hydrogen is displaced, methyl ether is formed—

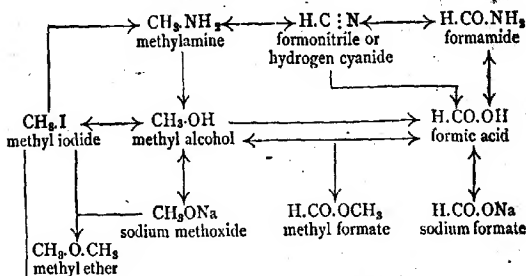


Hence metamerism (§ 51).

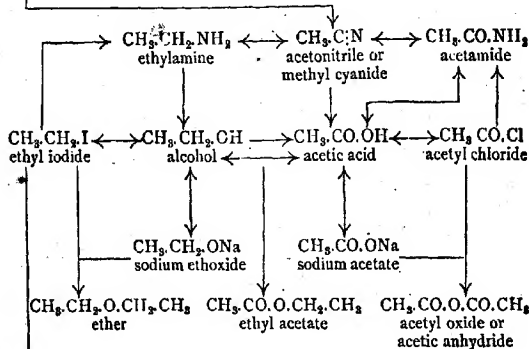
**70. Synopsis.**—The existence of several radicals in the same molecule leads to the assumption that the atoms are linked together in a definite manner. This structure or molecular constitution is deduced from the reactions of the compound, and the valency of its atoms. The formulæ thus obtained are termed structural or constitutional formulæ. They not only symbolise the chemical actions and relations of the substances, but also account for homology and isomerism.

## EXPERIMENTAL BASIS OF STRUCTURAL FORMULÆ.

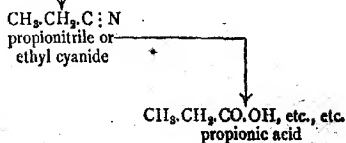
## I. THE METHYL-FORMIC GROUP.



## II. THE ETHYL-ACETIC GROUP.



## III. THE PROPYL-PROPIONIC GROUP.



[For structure of the higher fatty acids and alcohols, see § 80.]

### SECTION III

## THE SATURATED HYDROCARBONS AND THE THEORY OF SUBSTITUTION

### CHAPTER XIII

#### METHANE AND ITS SUBSTITUTION PRODUCTS

**71. Methane or Marsh-gas.**—The hydrocarbons are compounds which contain only carbon and hydrogen; they are of considerable importance in themselves, and especially interesting from their bearing on theory and classification.

The simplest hydrocarbon is the gas methane, which is formed when complex organic matter, such as wood or coal, is distilled destructively. Methane constitutes about 40 per cent. of ordinary illuminating gas; and is the active constituent of the explosive "fire-damp," which escapes from coal-seams. Fire-damp is sometimes nearly pure methane, and rarely contains less than 60 per cent. of the gas; the balance is mainly nitrogen.

Methane is also associated with petroleum, often in such quantity as to be forced from the wells under great pressure, as at Baku on the Caspian, and in Pennsylvania; it occurs somewhat similarly as "natural gas" at Heathfield in Sussex, and was first observed in the gases arising from marshes.

*Methane*,  $\text{CH}_4$  (Volta, 1777), is a light, insoluble gas, which when cooled by liquid air condenses to a very light, colourless liquid; it boils at  $-152^\circ$ , freezes at  $-186^\circ$ , and has a specific gravity about 0.4.

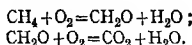
The gas burns with a pale flame to carbon dioxide and water (Volta), and explodes violently with air, forming the same products. The initial product, however, is formaldehyde,  $\text{CH}_2\text{O}$  (§ 86),\* which may be isolated in considerable

---

\* Or, possibly, methyl alcohol.



quantity when a mixture of methane and oxygen is heated at 450–500° (Bone, 1903); the carbon dioxide is formed, together with some carbon monoxide, by further oxidation of the formaldehyde.



Gaseous carbon compounds are analysed by combustion with oxygen: the following example will illustrate the principle of the method, but for details a work on gas analysis must be consulted.

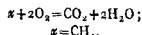
5 cc. of methane exploded with 19 cc. of oxygen gave 14 cc. of gas; this contracted to 9 cc. when shaken with caustic potash; the residue was completely absorbed by alkaline pyrogallol (§ 305).

The residual 9 cc. was oxygen (alkaline pyrogallol absorbs oxygen completely); hence the methane had combined with 10 cc. or twice its own volume of oxygen. The 5 cc. absorbed by caustic alkali (14–9=5) was carbon dioxide; hence the methane gave its own volume of this gas. The initial contraction of 10 cc. (5+19–14=10) was therefore due to the condensation of steam, of which the methane produced twice its own volume.

These results may be summarised as under—

$x$  vol. methane + 2 vols. oxygen gave 1 vol. carbon dioxide + 2 vols. steam;

and by Avogadro's law, if  $x$  be the molecule of methane,



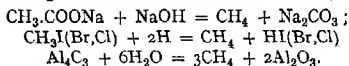
This molecular formula is confirmed by the density of the gas, which is eight times greater than that of hydrogen, giving a molecular weight of 16.

**72. Synthesis of Methane.**—Methane has been synthesised in many ways. It is formed in small quantities, when carbon is heated at 1200° in an atmosphere of hydrogen; and conversely, is partially resolved into its elements by prolonged sparking. It was first artificially prepared from acetic acid (Dumas, 1830). An intimate mixture of fused sodium acetate, soda-lime and iron-filings is heated to dull redness in a wide tube or small flask of hard glass, which is provided with a delivery tube; the methane which is generated contains free hydrogen, but is otherwise pure; the iron filings serve to conduct the heat.

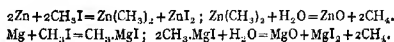
A more direct synthesis is effected by passing sulphuretted hydrogen, containing carbon bisulphide vapour, over red-hot copper turnings (Berthelot, 1856); the sulphur is taken up by the copper, whilst the hydrogen combines with the carbon; but the product is very impure. A better result is obtained by passing carbon monoxide with three times its volume of hydrogen over reduced nickel, which is heated at about 220°;

the carbon monoxide is converted quantitatively into methane and steam (Sabatier, 1902).

Methane is also formed by the action of water on aluminium carbide, a crystalline substance which is made by heating aluminium with carbon in an electric furnace (Moissan, 1894); and it can be made by reducing methyl iodide, either directly with nascent hydrogen, or indirectly through its compounds with metallic zinc or magnesium.

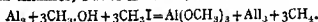


When methyl iodide is heated with zinc dust, it forms a volatile liquid, zinc methyl,  $\text{Zn}(\text{CH}_3)_2$  (§ 91); this is hydrolysed to zinc oxide and methane, when its solution in ether is allowed to drop into water (E. Frankland, 1856). Or water may be allowed to drop on zinc dust moistened with the calculated amount of methyl iodide, and heated at 50–100°. The zinc may with advantage be replaced by magnesium. Metallic magnesium dissolves with great energy in a mixture of methyl iodide and dry ether, forming *magnesium methiodide*,  $\text{CH}_3\text{MgI}$ ; on dropping water into the ethereal solution of this substance, methane is evolved in abundance (Grignard, 1900).



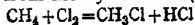
The methyl compound may also be reduced directly with nascent hydrogen, the reduction being conveniently effected electrolytically by means of a copper-zinc couple (Gladstone, 1874), or an aluminium mercury couple (Cohen, 1898). The aluminium-mercury couple is very energetic; it is made by coating small pieces of sheet aluminium with mercury, by covering them with a cold solution of mercuric chloride, and is washed with dry methyl alcohol (water is immediately attacked by the couple).

A mixture of methyl iodide and dry methyl alcohol is now dropped on the amalgam, which is packed in a U-tube cooled with ice, and is covered with methyl iodide; aluminium methoxide and aluminium iodide are formed, and methane is set free. The copper-zinc couple is made and used in a similar manner, but is much slower in action.



### 78. Chlorination of Methane: the Chloromethanes: Chloroform.

—Methane can not only be made from methyl compounds, but can be reconverted into them. When it is mixed with chlorine, and exposed to diffused daylight, a slow action takes place; the chlorine gradually disappears, and the gas becomes acid with hydrogen chloride; but there is no alteration in volume. On cooling the washed and dried vapour in a powerful freezing-mixture, it is found to be methyl chloride, identical with that prepared from methyl alcohol (Dumas, 1842).



Methane is therefore *methyl hydride*,  $\text{CH}_3\text{H}$ , and methyl chloride is derived from it by the substitution of chlorine for hydrogen. Methyl chloride is accordingly a substitution product of the hydrocarbon, and may be termed *chloromethane*. The replacement of hydrogen by chlorine is termed direct substitution, and that of chlorine by hydrogen, inverse substitution (Laurent, 1839).

If the chlorination be continued, or methyl chloride be directly chlorinated, the action proceeds in a similar manner

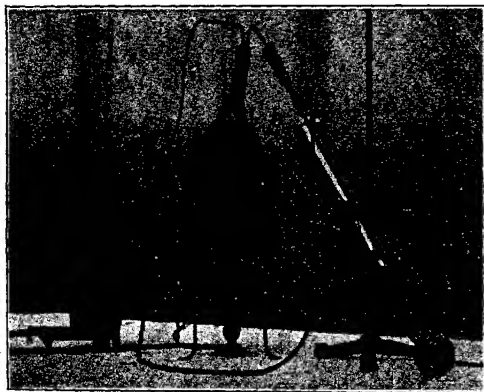


Fig. 15.—Preparation of Chloroform.

until eventually the whole of the methane hydrogen is replaced by chlorine (Regnault, 1840).

The dichloromethane, trichloromethane and tetrachloromethane thus formed are heavy, colourless liquids; and the second of these is the well-known anæsthetic, chloroform. Chloroform was first made by the action of bleaching-powder on acetone (Liebig, 1831, § 90) or ethyl alcohol (Souberain, 1831, § 115), and is still manufactured in this way.

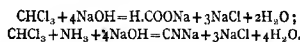
The bleaching-powder is made into a paste with water, and on adding the dilute spirit, and warming gently on a water-bath, a brisk action sets in. Part of the chloroform distils at once, and the remainder is expelled, either by boiling the product, or by distilling it in a current of steam (Fig. 15).

The crude distillate is shaken with dilute caustic soda, to neutralise acid and remove free chlorine, and the heavy chloroform having been separated with a tap-funnel is shaken with concentrated sulphuric acid to remove water and alcohol. It is then separated from the acid and redistilled; when made from acetone it is pure, but when made from alcohol it contains a little ethyl chloride. Chloroform may also be obtained by mixing chloral hydrate with caustic soda solution (Liebig, 1831; § 115).

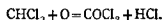
*Chloroform* or *trichloromethane*,  $\text{CHCl}_3$  (Liebig, Souberain, 1831), is a colourless liquid, having a powerful but not unpleasant odour, and a very sweet taste. It boils at  $61^\circ$ , and freezes at  $-60^\circ$ ; its specific gravity is 1.50 at  $15^\circ$ . Chloroform is extensively used as an anæsthetic (Simpson, 1848), and for this purpose is usually mixed with some alcohol (0.5 per cent.) to prevent the formation of carbonyl chloride (see below); the addition of a little ethyl chloride greatly accelerates the anæsthetic action.

Chloroform precipitates silver chloride when heated with alcoholic silver nitrate, and it further resembles the alkyl chlorides in that it is hydrolysed by alkalies; the products of hydrolysis are the alkali chloride and formate (whence its name).

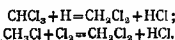
In presence of alkalies chloroform combines with ammonia, forming the alkali cyanide. Amines have a similar action, and the reaction with phenylamine or aniline, producing phenyl isocyanide (§ 256), affords a very delicate test for chloroform.



Chloroform is oxidised by chromic acid to a poisonous gas, carbonyl chloride (§ 192), and hydrogen chloride. The same change is slowly effected by air in daylight, so that pure chloroform must be kept in a cool dark place; the presence of a small quantity of alcohol, however, retards this oxidation enormously.



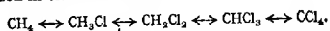
When chloroform is exposed to the action of nascent hydrogen, it is reduced ultimately to methane; but chloromethane and dichloromethane are formed as intermediate products. Dichloromethane is conveniently prepared by adding hydrochloric acid to zinc covered with chloroform and alcohol; it is also formed in the chlorination of methyl chloride. *Methyl-ene chloride* or *dichloromethane*,  $\text{CH}_2\text{Cl}_2$  (Regnault, 1840), is a heavy volatile liquid, which resembles chloroform, and boils at  $42^\circ$ .



By further chlorinating chloroform it is converted into carbon tetrachloride or tetrachloromethane; this is the final product of the chlorination of methane. It is best prepared by the action of chlorine on carbon

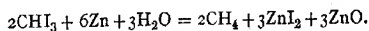
disulphide in presence of antimony pentachloride. *Carbon tetrachloride* or *tetrachloromethane*,  $\text{CCl}_4$  (Regnault, 1840), is a heavy, colourless liquid which boils at  $77^\circ$ . It is often used as a solvent in chlorinations, as it is unaffected by chlorine. Carbon tetrachloride is hydrolysed by alkalis in the same way as chloroform, the final product being the alkali carbonate.

When reduced with sodium amalgam in alcoholic solution, carbon tetrachloride is converted into chloroform, methylene chloride, etc., so that the chlorination products of methane form a continuous series, which can be traversed in either direction.



**74. The Bromomethanes and Iodomethanes: Bromoform and Iodoform.**—The iodine compound corresponding with chloroform is made in an analogous manner, by the action of iodine and alkali on alcohol or acetone. The iodine is added to a solution of sodium carbonate, containing the spirit, and the whole is warmed gently, the addition of iodine being continued until the colour ceases to be discharged; a relatively large quantity is required. On cooling the product, the yellow iodoform crystallises out; it is washed with a little cold water, and dried on a porous plate. It may be crystallised from acetone in large, transparent, hexagonal tablets.

*Iodoform* or *triiodomethane*,  $\text{CHI}_3$  (Serullas, 1822), is a bright yellow, crystalline substance, which melts at  $119^\circ$ , and sublimes slowly when gently heated; it is readily volatile with steam. Iodoform has a clinging and characteristic odour, and is used in surgery as an antiseptic. It is hydrolysed by alcoholic alkali in the same way as chloroform, and when heated with zinc dust and water is reduced to methane. When iodoform is heated strongly, much iodine is set free. The mechanism of the formation of iodoform (§§ 90, 115) is complicated.



*Bromoform* or *tribromomethane*,  $\text{CHBr}_3$  (Löwig, 1832) is a very heavy and somewhat unstable liquid, which boils at  $151^\circ$ , and freezes at  $7^\circ$ ; its specific gravity is 2.9. It is made by the action of sodium hypobromite on acetone, and is decomposed by alkalis in a complicated manner.

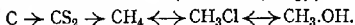
Substitution by bromine is effected with greater difficulty than by chlorine, and with iodine direct substitution is only possible in exceptional cases. On the other hand the bromo- and iodo-compounds are more easily reduced than the chloro-compounds. The volatility and fusibility of the halogen derivatives of methane vary inversely with the number of halogen atoms, and the atomic weight of the halogen.

## HALOGEN SUBSTITUTION PRODUCTS OF METHANE.

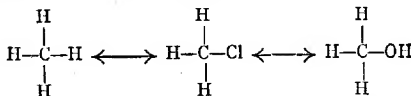
Methane: B.p.  $-152^{\circ}$ ; m.p.  $-186^{\circ}$ .

Substitution Product.	Fluoro.	Chloro.		Bromo.		Iodo.	
		B.p.	M.p.	B.p.	M.p.	B.p.	M.p.
Mono-	gas	$-23^{\circ}$	$-104^{\circ}$	$-4^{\circ}$	—	$43^{\circ}$	—
Di . .	gas	$+42^{\circ}$	—	$97^{\circ}$	—	$180^{\circ}$	$+4^{\circ}$
Tri . .	gas	$61^{\circ}$	$-60^{\circ}$	$146^{\circ}$	$+9^{\circ}$	decomp.	$119^{\circ}$
Tetra-	gas	$77^{\circ}$	$-30^{\circ}$	$189^{\circ}$	$92^{\circ}$	decomposed.	

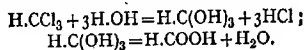
**75. Methyl Alcohol and its Oxidation Products: Hydroxymethanes.**—Chloromethane, made from methane, is identical with methyl chloride made from methyl alcohol, and is accordingly convertible into this alcohol by hydrolysis. The gas is dissolved in caustic potash, and heated in a sealed tube; and the volatile product of the action, when purified, is identical with rectified wood spirit. The synthesis of methyl alcohol was thus first effected (Berthelot, 1857).



It follows from this double identity that methyl alcohol is a substitution product of methane, or *hydroxymethane*; it is methane in which one-fourth of the hydrogen is replaced by hydroxyl (compare § 71, footnote).

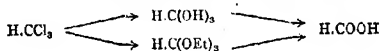


Similarly, formic acid is a dehydrated trihydroxymethane, corresponding with chloroform, and carbon dioxide a dehydrated tetrahydroxymethane. The first product formed in the hydrolysis of chloroform is *orthoformic acid*,  $\text{CH}(\text{OH})_3$ ; but this cannot exist in the free state, and loses water, giving ordinary formic acid. Hence when chloroform is boiled with aqueous alkalis the alkali formate is produced.

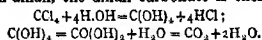


If the reaction is carried out in alcoholic solution, esters of orthoformic acid are obtained. When chloroform is mixed with an alcoholic solution of sodium ethoxide (i.e. sodium dissolved in excess of alcohol), there is a vigorous action, and a light, oily layer of ethyl orthoformate forms on the surface of the liquid. This can be separated, dried and distilled. *Ethyl orthoformate*,  $\text{H.C}(\text{OEt})_3$  (Williamson, 1854), is a liquid which boils at  $146^{\circ}$ .

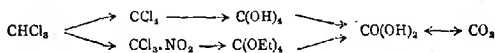
When heated with aqueous alkali, it is readily hydrolysed to alcohol and the alkali formate. The corresponding *methyl orthoformate* boils at  $102^{\circ}$ . Formic acid is thus the representative of *trihydroxymethane*.



The tetrahydroxy-methane, corresponding with carbon tetrachloride and carbonic acid, cannot exist in the free state, and breaks up successively into carbonic acid and carbon dioxide. When carbon tetrachloride is hydrolysed with alkali, the alkali carbonate is therefore produced.

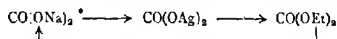


The esters of orthocarbonic acid cannot be prepared directly from carbon tetrachloride, but they are formed in an analogous manner, by the action of alcoholic potash on trichloronitromethane, (§ 233), a substance which is obtained by the action of nitric acid on chloroform. *Ethyl orthocarbonate*,  $\text{C(OEt)}_4$  (Basset, 1864), is a liquid which boils at  $168^{\circ}$ ; it is easily hydrolysed by alkalis to alcohol and the alkali carbonate.



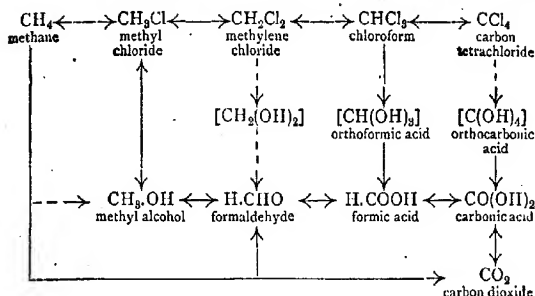
Carbon dioxide is thus the representative of *tetrahydroxymethane*, and the unstable carbonic acid of the ordinary carbonates is an intermediate dehydration product.

Carbonic acid is so feeble an acid that its esters cannot be formed by direct interaction with the alcohols. They are readily obtained by digesting silver carbonate with the alkyl iodide, in the same way as ethyl acetate from silver acetate and ethyl iodide; they are also formed by the prolonged interaction of the alcohols with carbonyl chloride, in the same way as in the preparation of ethyl acetate from alcohol and acetyl chloride. *Ethyl carbonate*,  $\text{CO(OEt)}_2$  (Clermont, 1854), is a liquid which boils at  $126^{\circ}$ ; it is hydrolysed by alkalis to alcohol and the alkali carbonate.



It will be shown later (§ 86) that formaldehyde, the product intermediate to methyl alcohol and formic acid, represents dihydroxymethane, and corresponds with methylene chloride. The oxidation products of methane therefore form a series parallel to the chloro-substitution products, and comprise all the hydroxymethanes which are possible, according to the theory of structure and valency.

Hence the ultimate oxidation product of methane, whether formed by direct oxidation, or indirectly through the chlorination products, is tetrahydroxymethane, which corresponds with the carbon dioxide obtained in actual practice.



**76. Synopsis.**—Methyl chloride is identical with chloro-methane, a chloro-substitution product of the hydrocarbon, methane or marsh-gas. Methyl alcohol is the corresponding hydroxy-methane. The oxidation products of methyl alcohol correspond with the higher chloro-substitution products of methane, and represent all the hydroxy-methanes which are theoretically possible.



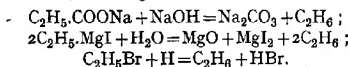


## CHAPTER XIV

### THE PARAFFINS : CHAIN ISOMERISM

**77. Ethane.**—Methane is the first member of a series of hydrocarbons, which are related to ethyl alcohol, acetic acid and their homologues in the same way as methane itself to methyl alcohol and formic acid. Like methane, these hydrocarbons occur in nature ; they form the chief constituents of paraffin oil or petroleum.

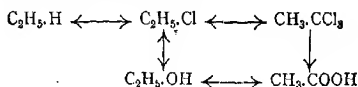
*Ethane, the hydrocarbon corresponding with ordinary alcohol and acetic acid, occurs together with methane at Pittsburg, U.S.A., where it is utilised for lighting, heating, etc. It may be prepared synthetically from ethyl bromide or iodide, or propionic acid, by the methods which have been described under methane, which gas it resembles in all essential details.*



*Ethane, CH<sub>3</sub>.CH<sub>3</sub> (Frankland, 1848), is an insoluble gas, which is somewhat heavier than air. When cooled sufficiently it condenses to a very light, colourless liquid, which boils at -85°, freezes at -171°, and has a specific gravity of 0.45. It burns with a somewhat luminous flame to carbon dioxide and water ; and as with methane, the initial product of oxidation is the aldehyde, or compound intermediate to the corresponding alcohol and acid (§ 82).*

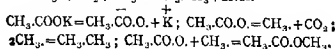
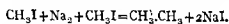
Like methane, ethane has practically no action on bromine water ; but when mixed with chlorine in daylight, it is slowly converted into substitution products. *Monochlorethane* is identical with ethyl chloride, and convertible into ethyl alcohol by hydrolysis ; ethane is therefore *ethyl hydride*, and alcohol, *hydroxyethane*. By further chlorination, *trichlorethane*, CH<sub>3</sub>.CCl<sub>3</sub>, is obtained, which resembles chloroform, and is converted into acetic acid when hydrolysed ; it may also be

converted into *ethyl orthoacetate*,  $\text{CH}_3\text{C}(\text{OEt})_3$ , a liquid analogous to ethyl orthoformate. Acetic acid is therefore the representative of *trihydroxyethane*.



Ethane is more complex than methane, and may also be regarded as *dimethyl*; it was first obtained in fact in an attempt to isolate the methyl radical. When methyl iodide is heated with excess of zinc (Frankland, 1840) or sodium (Wurtz, 1855), the iodine is removed in combination with the metal, and the methyl groups unite with one another, forming dimethyl or ethane; in presence of acetonitrile the action proceeds at the ordinary temperature. Similarly, when a strong solution of potassium acetate is electrolysed, methyl radicals are set free by the decomposition of the acetoxy ions,  $\text{CH}_3\text{COO}$ , at the anode. These in turn unite with one another, forming dimethyl or ethane (Kolbe, 1849); but some combine with undecomposed acetoxy ions, forming methyl acetate.

The ethane formed from methyl compounds in these ways is identical with that prepared from ethyl compounds, and is convertible into ethyl chloride and ethyl alcohol in the same manner (Schorlemmer, 1862):



#### 78. The Methane or Paraffin Series: Saturated Compounds.—

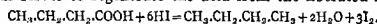
The character of the hydrocarbons of the methane series changes with increase of molecular weight, in the same way as that of the alcohols and acids derived from them. The volatility diminishes; gases become liquids; volatile liquids pass into liquids of high boiling-point, and eventually into solids.

These hydrocarbons are essential constituents of ordinary petroleum, from which many of them may be isolated by fractional distillation (Pelouze, Williams, Schorlemmer, 1857-64); the higher members of the series are light, insoluble liquids, or easily fusible solids, and the more volatile are characterised by a fresh, ethereal odour (the peculiar odour of paraffin oil is due to impurities).

*Propane*,  $\text{C}_3\text{H}_8$ , which is formed in the same way as ethane, is a heavy gas, which condenses to a light liquid at  $-37^\circ$ . *Butane*,  $\text{C}_4\text{H}_{10}$ , which is made by heating ethyl iodide with excess of zinc or sodium, is a light, very volatile liquid, boiling at  $+1^\circ$ . *Pentane*,  $\text{C}_5\text{H}_{12}$ , boils at  $36^\circ$ , and is used as a standard of illuminating power. *Hexane*,  $\text{C}_6\text{H}_{14}$ , boils at  $69^\circ$ , and can be prepared from the natural sugars. *Heptane*,  $\text{C}_7\text{H}_{16}$ , boils at

98°, and is obtained on distilling Californian pine resin.

From butane upwards, these hydrocarbons can be made by heating the corresponding acids with fuming hydriodic acid and red phosphorus (Berthelot, 1867). Hydriodic acid at the high temperature employed is resolved into iodine and hydrogen, which under these conditions is the most powerful reducing agent applicable to carbon compounds. The phosphorus serves to regenerate the acid from the liberated iodine.



The homologous compounds up to pentadecane steadily decrease in volatility. *Hexadecane*,  $\text{C}_{16}\text{H}_{34}$ , the hydrocarbon corresponding with palmitic acid, is a crystalline solid, which melts at 18°, and boils at 257°. *Octadecane*,  $\text{C}_{18}\text{H}_{38}$ , corresponding with stearic acid, melts at 28°, and boils at 317°. The highest known member of the methane series is the *hydrocarbon*,  $\text{C}_{90}\text{H}_{182}$ , a crystalline solid melting at 102°.

The methane hydrocarbons are distinguished by their great inertness towards ordinary chemical agents; they do not decolorise bromine water, nor reduce alkaline permanganate; and although they are attacked by chlorine, the action is very slow. On account of this general inertness, they are known as the *paraffins* (Watts, 1873).\*

Compounds such as these, which act only by substitution, and do not enter into additive combinations (§§ 85, 104), are termed saturated compounds. The carbon atom is never more than quadrivalent, and when the four valencies are already saturated, hydrogen must be displaced to make room for the new atom or group.

The paraffins do not unite directly with other substances, but they are eventually reconvertible into alcohols, acids, etc., by methods of chlorination, hydrolysis and oxidation, analogous to those employed with methane and ethane (§§ 75, 77). The fatty compounds in general are therefore substituted paraffins (§ 81).

The practical details of this reversion are simpler than with the gaseous hydrocarbons, because liquids and solids are more easily handled than gases; but the results are identical. Chlorine is the most effective agent, although others, such as sulphuric acid and nitric acid (§§ 231, 246) are also occasionally employed.

**79. Petroleum: Paraffin Oil and Wax.**—Petroleum or rock oil has been known for many centuries; the oily scum, which sometimes floats on the surface of wells, was used as a healing ointment by the Romans and North American Indians. The first discovery of petroleum in quantity was made in Derbyshire in the middle of the last century (Playfair, 1847), when a

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\* *Parum affinis* (Reichenbach, 1839); the name was originally given to a solid, waxy member of the series, obtained by distilling wood-tar,

rich spring of dense oil was found in a disused mine. This spring was soon exhausted, and various methods were tried of making the oil artificially. The most successful of these, which is still used, consists in distilling cannel coal or shale—slate-coal (Young, 1848).

Soon afterwards oil was struck in Pennsylvania, and in 1861 a well was bored, from which crude petroleum flowed spontaneously at the rate of 100,000 gallons a day. Since then, petroleum has been found in various parts of the world. It is probable that natural oil, the supply of which in many districts seems inexhaustible, is formed by the action of water on natural metallic carbides (Mendeléeff, 1877); uranium carbide thus gives a mixture of gaseous, liquid and solid hydrocarbons when hydrolysed.

Petroleum, whether natural or artificial, is a complex mixture; besides members of the paraffin series, there are also present naphthenes (§ 287), aromatic hydrocarbons (§ 242), and olefines (§ 106). Russian and Galician petroleum is especially rich in naphthenes, and shale oil in olefines; American petroleum also contains these, as well as aromatic hydrocarbons, but the paraffins predominate.

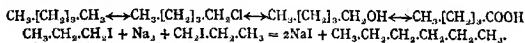
Crude petroleum is a dark, viscid, malodorous liquid, and is useless until it has been refined by fractionation and chemical purification. The oil is first roughly distilled, to separate pitchy substances. The distillate is agitated with caustic alkali to remove acid impurities (phenols, § 254), and then with concentrated sulphuric acid to separate basic impurities, colouring matter, and to a certain extent, hydrocarbons of other series. It is then fractionated.

Dissolved gaseous hydrocarbons from methane to butane having been expelled, the distillate is collected. The most volatile fraction, *petroleum ether*, *petrol* or *motor-spirit*, boils at 30–100°, and has a specific gravity of 0.6–0.7; it consists largely of pentane, hexane and heptane. The succeeding fraction is used in spirit lamps, as *heptoline*. Ordinary *illuminating oil* boils at 150–280°, and has a specific gravity of 0.8–0.85; it contains the paraffins from nonane to hexadecane. Paraffin oil is dangerous when it “flashes” or gives an inflammable vapour below 40°, and numerous lamp explosions are caused by the use of cheap oil of low flash-point. The fractions boiling at 300° and upwards are more or less viscid, and form *lubricating oil*. At a still higher temperature the distillate becomes semi-solid, and is known as *vaseline*. The final fractions set to a crystalline solid, *paraffin wax*; commercial solid paraffin contains the hydrocarbons  $C_{25}H_{52}$  and upwards.

**80. Constitution of the Paraffins: Iso-Paraffins: Chain Isomerism.**—The constitution of the ordinary or *normal paraffins* follows from their conversion, by successive chlorination and hydrolysis, into the corresponding alcohols and acids (Schorlemmer, 1883), and from their synthesis from the lower alkyl iodides (§ 77) by the Wurtz reaction (Schorlemmer, 1872).

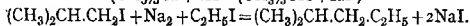
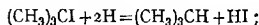
When normal pentane, the pentane of highest boiling point, is chlorinated, an amyl chloride is obtained, which is convertible into amyl alcohol and valeric acid. The constitutional formula of valeric acid,  $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot COOH$ , is proved by the cyanide synthesis, and normal pentane is therefore represented by the formula  $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_3$ . Normal **hexane** can be prepared synthetically by the action of sodium on the

propyl iodide made from ordinary propyl alcohol ; hence it is *dipropyl*,  $[\text{CH}_2\text{CH}_2\text{CH}_2]_2$ , just as normal butane and ethane are diethyl and dimethyl respectively.

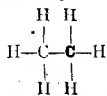


But besides these normal paraffins, corresponding with the ordinary alcohols and acids, petroleum contains more volatile isomeric compounds, some of which have been isolated by careful fractionation of American petroleum ; they were first obtained synthetically, from the corresponding iso-halogen derivatives (§§ 97, 99).

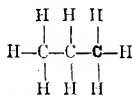
*Isobutane*,  $\text{C}_4\text{H}_{10}$ , a gas condensing at  $-6^\circ$ , is formed by digesting tertiary-butyl iodide (§ 98) with zinc and water. *Isopentane*,  $\text{C}_5\text{H}_{12}$  (Frankland, 1850), a light liquid boiling at  $30^\circ$ , is formed similarly from isoamyl iodide. *Isohexane*,  $\text{C}_6\text{H}_{14}$  (Wurtz, 1855), which boils at  $62^\circ$ , is formed by the action of sodium on a mixture of isobutyl iodide (§ 97) and ethyl iodide, in the same way as ethane from methyl iodide.



There are no isomerides of ethane and propane : the carbon atoms are necessarily linked together, and the remaining valencies are satisfied by the hydrogen atoms.

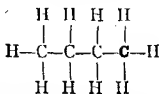


Ethane or Methyl-methane.

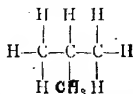


Propane or Methyl-ethane.

But the structural formula of butane may be arranged in two ways ; the fourth carbon atom may be linked with either a terminal or a median atom of the propane nucleus.



Normal butane or Di-ethyl.



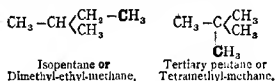
Isobutane or Trimethyl-methane.

The first formula corresponds with normal butane, the molecule of which contains two ethyl radicals. Isobutane is therefore represented by the second formula, and must be regarded as *trimethyl-methane*,  $\text{CH}(\text{CH}_3)_3$ .

With the pentanes the possibilities are still greater. The fifth carbon

atom may be linked to a terminal or median atom of the normal butane nucleus, giving formulæ which correspond with normal pentane, and *dimethyl-ethyl-methane*,  $\text{CH}(\text{CH}_3)_2 \cdot \text{C}_2\text{H}_5$ . As isopentane is made from isoamyl iodide, which has the constitution  $\text{CH}(\text{CH}_3)_2 \cdot \text{CH}_2 \cdot \text{CH}_2\text{I}$  (§ 99), it is identical with this theoretically deduced dimethyl-ethyl-methane.

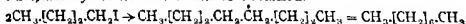
But two pentanes may be derived similarly from isobutane, the fifth carbon atom being linked either to the carbon of one of the methyl groups, or to the central carbon atom. In the first place, the formula is again that of dimethyl-ethyl-methane, but in the second case, it is that of a new combination, tetramethyl-methane,  $\text{C}(\text{CH}_3)_4$ .



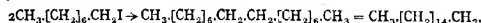
The third or tertiary pentane has been made synthetically, by the action of zinc methyl on tertiary butyl iodide,  $\text{C}(\text{CH}_3)_3\text{I}$  (§ 98). *Tertiary pentane* or *tetramethyl-methane*,  $\text{C}(\text{CH}_3)_4$  (Lwow, 1870), is a very volatile liquid, which boils at  $9^\circ$ , and freezes at  $-20^\circ$ .

The possibility of isomerism rapidly increases with the number of carbon atoms. There are five hexanes, nine heptanes, and eighteen octanes possible theoretically; and the formula of *tridecane*,  $\text{C}_{13}\text{H}_{28}$ , can be arranged in upwards of 800 distinct ways. The five hexanes are known, and five of the nine heptanes, but above this point the isomerism of the paraffins has not been tested experimentally.

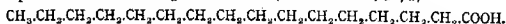
In a few special cases the constitution of individual paraffins has been established synthetically (see also § 94). By heating butyl iodide with zinc-dust, *dibutyl* or *normal octane* is obtained.



The primary octyl iodide derived from this octane is convertible into *dioctyl* or *normal hexadecane*.



This hexadecane is identical with that which is obtained by reducing palmitic acid with hydriodic acid; and palmitic acid is therefore a normal compound of the following constitution (Schorlemmer, 1872).



The isomerism of the paraffins depends on the ability of the carbon atoms to unite with one another, and on their rigid quadrivalence. It is known as *chain isomerism*. The carbon atoms of the normal paraffins (of relatively the highest boiling-point) are connected in a continuous or *normal* chain, whilst those of the iso- and tertiary paraffins are linked in branching chains. The derivatives of these paraffins will be studied later (§§ 97-99).

**81. Synopsis.**—The saturated hydrocarbons homologous with methane, from which the ordinary alcohols and acids are derived, occur in petroleum, and are termed paraffins, from their chemical inertness. The higher paraffins exist in numer-

ous isomeric forms, in which the carbon atoms are linked in branching chains.

THE NORMAL PARAFFINS AND THEIR OXYGENATED DERIVATIVES

Hydrocarbon $C_n H_{2n+2}$	Alcohol $C_n H_{2n+1} \cdot OH$	Acid $C_n H_{2n} O_2 = C_n - H_{2n-2} \cdot COOH$
Methane (−164°) [−186°]	Methyl (65°) [−94°]	Formic (101°) [9°]
Ethane (−84°) [−171°]	Ethyl (78°) [−112°]	Acetic (118°) [16°]
Propane (−37°)	Propyl (97°) [−127°]	Propionic (141°) [−19°]
Butane (1°)	Butyl (117°)	Butyric (162°) [−8°]
Pentane (37°)	Amyl (138°)	Valeric (186°) [−58°]
Hexane (69°)	Hexyl (157°)	Caproic (205°) [−1°]
Heptane (98°)	Heptyl (176°)	Oenanthylic (224°) [−10°]
Octane (125°)	Octyl (196°)	Caprylic (237°) [17°]
Nonane (149°) [−51°]	Nonyl (214°) [−15°]	Pelargonic (254°) [12°]
Decane (174°) [−31°]	Decyl (231°) [7°]	Capric (269°) [30°]
Undecane (197°) [−26°]	—	Undecolic [28°]
Dodecane (216°) [−12°]	Dodecyl [24°]	Lauric [44°]
Tridecane (234°) [−6°]	—	Tridecoic [41°]
Tetradecane (252°) [6°]	Tetradecyl [38°]	Myristic [54°]
Pentadecane (270°) [10°]	Pentadecyl [46°]	Pentadecolic [51°]
Hexadecane (287°) [18°]	Cetyl [49°]	Palmitic [62°]
Heptadecane (303°) [23°]	—	Margaric [60°]
Octadecane (317°) [28°]	Stearyl [59°]	Stearic [69°]
Nonadecane (330°) [32°]	—	Nonadecolic [67°]
Bicosane — [37°]	—	Arachidic [77°]

The higher alcohols and acids whose boiling-points are not given can be distilled unchanged only under reduced pressure.



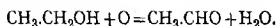
## SECTION IV

### THE THEORY OF STRUCTURE DEVELOPED

#### CHAPTER XV

##### THE ALDEHYDES

**82. Oxidation of Alcohol and Reduction of Acetic Acid to Aldehyde.**—When alcohol is oxidised with a mild agent, such as chromic acid, or manganese dioxide and dilute sulphuric acid, an intermediate product, aldehyde, is obtained, instead of the acetic acid, which is formed when a more energetic agent is employed (Scheele, 1774).



To obtain this product in quantity, a cold mixture of alcohol and dilute sulphuric acid is allowed to drop on crystallised potassium dichromate, which is placed in a large flask, connected with a reflux condenser supplied with warm water (Fig. 16); a brisk action occurs, the chromate is reduced to chrome alum, and the volatile aldehyde distils over, whilst any unchanged alcohol is returned to the flask.

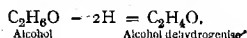
It is best isolated in the form of a crystalline derivative, aldehyde-ammonia (Döbereiner, 1821).

The crude aldehyde vapour is absorbed in dry ether, contained in a Volhard trap (compare Fig. 18, § 114), which is kept cool by ice-water; and at the end of the operation it is converted into aldehyde-ammonia by saturating the ethereal solution with dry ammonia gas.

On distilling the air-dried aldehyde-ammonia with a slight excess of dilute sulphuric acid, at as low a temperature as possible, pure aldehyde volatilises; the vapour is dried with warm calcium chloride, and condensed in a freezing-mixture, the practical details being similar to those involved in the preparation of pure ethylamine (Fig. 14, § 57).

**Acetaldehyde**,  $\text{CH}_3\text{CHO}$  (Liebig, 1835), is a colourless, mobile very volatile liquid, which has a characteristic, suffo-

cating odour, and burns with a luminous flame; it boils at  $21^{\circ}$ , freezes at  $-121^{\circ}$ , and has a specific gravity of 0.801 at  $0^{\circ}$ . The empirical and molecular formula is  $C_2H_4O$ , so that its molecule is formed from that of alcohol by the removal of two hydrogen atoms (*alcohol dehydrogenatus*).



Aldehyde is also formed as an intermediate product in the reduction of acetyl chloride to alcohol by sodium amalgam (§ 36), and can be detected in the product during the earlier stages of the operation; the yield, how-

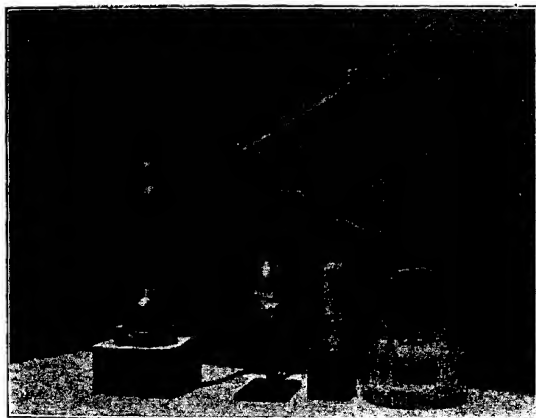
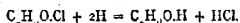


Fig. 16.—Preparation of Aldehyde-Ammonia.

When the dichromate is exhausted the ether-trap is disconnected from the reflux condenser, connected with the ammonia generator, and saturated with ammonia, while a fresh charge of dichromate is introduced into the flask. In the above operation the second charge of aldehyde is passing over.

ever, is very small, as most of the product at once undergoes further reduction (§ 83).

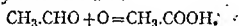


Aldehyde is also obtained by reducing acetic acid with formic acid, by means of the barium salts, which are made by neutralising the acids with barium carbonate. The calculated quantities are dissolved in water and evaporated to dryness together, and the intimate mixture thus prepared is distilled from a hard glass tube (Fig. 17, § 88); the distillate is

collected in water. The residue consists of barium carbonate, produced by oxidation of the formate (Piria, 1856).

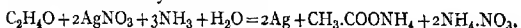


**83. Oxidation of Aldehyde to Acetic Acid and its Reduction to Alcohol.**—Aldehyde is a very unstable substance. It is oxidised to acetic acid even by prolonged exposure to air, and when warmed with acid permanganate is converted rapidly and quantitatively into this acid.

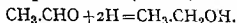


The aldehyde solution is cautiously poured down the condenser of a reflux apparatus containing the acid mixture, and after the violent action has moderated, more acid and permanganate are added, the boiling being continued until the agent ceases to be decolorised; the product is then filtered, and the acetic acid distilled off.

Being so readily oxidisable, it has marked reducing powers, and when warmed with ammoniacal silver nitrate in a test-tube, which is immersed in a beaker of hot water, it precipitates silver as a brilliant mirror on the sides of the tube (Liebig); the ammonia serves to neutralise the acetic and nitric acids as they are formed.

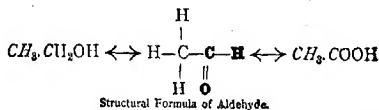


Conversely, aldehyde is reduced to alcohol by digestion with sodium amalgam and dilute sulphuric acid; after a few hours the characteristic odour disappears, and on distilling the product, dilute alcohol passes over (Wurtz, 1862).



A very characteristic property of aldehyde is its action on decolorised rosaniline; a solution of rosaniline hydrochloride (magenta dye) is bleached by a large excess of sulphurous acid, owing to the formation of a colourless compound, but on adding a little aldehyde, a violet colour appears (Schiff, 1867).

**84. Constitution of Aldehyde.**—As aldehyde is intermediate to alcohol and acetic acid, it contains the nucleus  $\text{CH}_3.\text{C}$ , and as the remaining three valencies can only be satisfied by direct attachment of the remaining hydrogen and oxygen atoms, its structural formula is as under.



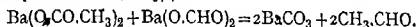
The aldehyde molecule thus consists of a methyl group

linked to a univalent radical,



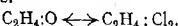
The Aldehyde Group or Radical.

This aldehyde group is identical with the formyl radical, and accounts for the reducing power of formic acid, and the formation of aldehyde from barium acetate and formate (Williamson, 1857).

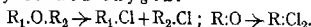


The constitution of aldehyde is confirmed by the action of phosphorus pentachloride, which converts it into a dihalogen product, ethylidene chloride; both acidic and alkylic hydroxyl are therefore absent (compare § 34). The absence of the latter is also proved independently by the indifference of aldehyde towards acetyl chloride (§ 41).

*Ethylidene chloride*,  $\text{CH}_3.\text{CHCl}_2$ , is a heavy, colourless liquid, which boils at  $60^\circ$ , and has a sweet odour and taste. When heated in a sealed tube with dilute sulphuric acid, it is reconverted into aldehyde.

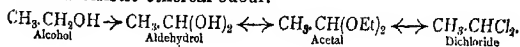


The two chlorine atoms thus reciprocally interchangeable with the aldehyde oxygen are necessarily linked to carbon, and the oxygen of aldehyde is therefore linked to carbon by both its valencies. As phosphorus pentachloride behaves with ethers and ethereal salts in the same way as with alcohols and acids, it serves to differentiate singly-linked from doubly-linked oxygen.



Although aldehyde itself does not contain hydroxyl, certain derivatives are known, which prove that it is the immediate representative of a dihydroxy-compound. Thus, on heating it with alcohol, or ethylidene chloride with sodium ethoxide, a kind of double ether, acetal, is formed.

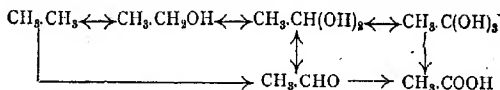
*Acetal or ethylidene diethyl ether*,  $\text{CH}_3.\text{CH}(\text{OEt})_2$  (Liebig, 1831), is a stable, neutral liquid, which boils at  $104^\circ$ , and has a characteristic ethereal odour.



The constitution of acetal is proved, not only by its formation from ethylidene chloride, but by its rapid hydrolysis to aldehyde and alcohol by dilute acids. The formation of aldehyde by oxidation is evidently preceded by that of a dihydroxy-compound or *aldehydrol*; in some cases such aldehydrols can actually be isolated (see Chloral, § 115).

Aldehyde is thus the representative of a *dihydroxyethane* intermediate between hydroxyethane or alcohol and trihydroxyethane or acetic acid; it is in fact the initial product of

the direct oxidation of ethane by oxygen at 500° (Bone, 1904).



85. **Additive Compounds, Polymerides, and Condensation Products of Aldehyde.**—The crystalline *aldehyde-ammonia*,  $\text{CH}_3\text{CHOH.NH}_2$ , used in the purification of aldehyde, is formed by direct union of the two molecules, and is a simple additive compound. A second compound of the same class, *aldehyde sodium sulphite*,  $\text{CH}_3\text{CHOH.SO}_3\text{Na}$  (Bertagnini, 1855), also a crystalline substance, is formed when pure aldehyde is shaken with a saturated solution of sodium hydrogen sulphite; like the ammonia compound, it is readily hydrolysed to its constituents.

An additive compound of a different type, *aldehyde hydrocyanide*,  $\text{CH}_3\text{CHOH.CN}$  (Gautier, 1867), a liquid boiling at 183°, is formed when aldehyde is gently heated with concentrated hydrocyanic acid in a closed vessel; it differs from the preceding compounds in that only part of the added molecule, namely the nitrogen, is detached by acid hydrolysis, the cyanogen being converted into carboxyl as in the simple nitriles (see Lactic Acid, § 137). Alcohol and acetic acid may themselves be regarded as additive derivatives of aldehyde.

The tendency of aldehyde to form additive compounds is so marked that it will even combine with itself. When a drop of concentrated sulphuric acid is added to the pure liquid, contraction takes place, much heat is evolved, and the boiling point rises many degrees, owing to the formation of a much less volatile isomeride termed *paraldehyde*, whilst if the temperature is kept below 0°, the aldehyde is converted into a white crystalline solid termed *metaldehyde*. Metaldehyde is also formed when aldehyde is kept in contact with calcium chloride.

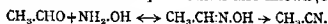
*Paraldehyde*,  $\text{CHMe} \begin{smallmatrix} \text{O.CHMe} \\ \text{O.CHMe} \end{smallmatrix} \text{O}$ , is a sparingly soluble liquid which boils at 124°; its molecular formula,  $\text{C}_6\text{H}_{12}\text{O}_3$ , follows from its vapour density. Unlike aldehyde, it is a stable substance, and is oxidised and reduced only with difficulty; it does not reduce silver, nor colour bleached rosaniline. It is converted into ethylidene chloride by phosphorus pentachloride, and reconverted into ordinary aldehyde when heated in a sealed tube with dilute sulphuric acid; and is thus a complex ether of the same type as acetal (Kekulé, 1870).

*Metaldehyde*,  $(\text{C}_2\text{H}_4\text{O})_3$ , is a white crystalline substance, which commences to sublime at about 115°, and at the same time is partially reconverted into ordinary aldehyde. Metaldehyde resembles paraldehyde in its actions, and is probably stereoisomeric with it (§ 141).

An internal additive compound of a different type, termed *aldol*, is formed by digesting aldehyde with aqueous potassium carbonate. *Aldol*,  $\text{C}_4\text{H}_8\text{O}_2$ , is a liquid of complex constitution (§ 146), resembling aldehyde in its general actions. These internal compounds are necessarily isomeric with aldehyde, and their molecules are simple multiples of the aldehyde molecule; such multiple isomerides are termed *polymerides* (Berzelius, 1831).

Whilst aldehyde acts initially almost entirely by addition, the additive compounds may undergo further change. Thus when aldehyde is mixed with hydroxylamine hydrochloride solution, and the hydroxylamine is set free by addition of sodium carbonate, the two substances coalesce, and at the same time lose water. The compound thus formed is isolated by shaking the product with ether; it is freely soluble in this liquid, but the ethereal solution is insoluble in water, and can be separated with a tap-funnel; the ether is then distilled off,

*Acetaldoxime*,  $\text{CH}_3\text{CH:N.OH}$  (V. Meyer, 1882), is a crystalline solid, which melts at  $47^\circ$  and boils at  $125^\circ$ ; it is reconverted into aldehyde and hydroxylamine by hydrochloric acid, and is dehydrated to acetonitrile by acetic anhydride. An unstable liquid form is also known (compare § 356).



An analogous compound, *aldehyde-phenyl-hydrazone*,  $\text{CH}_3\text{CH:N.NH.C}_6\text{H}_5$  (Fischer, 1885), an insoluble, oily liquid, which becomes crystalline after dissolving in strong alcohol, is formed by mixing solutions of aldehyde and phenyl-hydrazine acetate (§ 261); it is reconverted into its constituents by hydrolytic agents.



Compounds thus formed by the union of two molecules with elimination of water, or other simple product, are termed condensation products (compare § 146); when water itself is eliminated, as in these particular cases, condensation is the exact reverse of hydrolysis.

Aldehyde forms condensation products with itself. *Crotonaldehyde*,  $\text{C}_4\text{H}_7\text{CHO}$  (§ 133), is formed by the action of zinc chloride on aldol, or by simply distilling it. An action which is possibly similar is brought about by warming aldehyde with strong caustic soda solution; the *aldehyde resin* (Döbereiner, 1821) which is formed, is a sticky yellowish substance, having a characteristic soapy and resinous odour; little is known of its chemical nature, as it cannot be crystallised or distilled (see Isophthalic Acid, § 325).

The tendency of aldehyde to form these additive and condensation products is highly characteristic, and as will be seen later, actions of this kind play a very important part in the natural synthesis of organic compounds in plants.

**86. The Aldehydes.**—Like alcohol and acetic acid, aldehyde is the type of a large class of compounds, each pair of alcohols and acids being connected by a similar product. These intermediate compounds are termed, generically, the aldehydes, and are named after the corresponding acids.

The most conspicuous is formaldehyde, the product intermediate to methyl alcohol and formic acid. It is produced in small amount by the slow combustion of methane (§ 75), but is best prepared by the oxidation of methyl alcohol.

Dry air, charged with vapour from the latter at  $40^\circ$ , is led over a short spiral of copper gauze, which is heated to incipient redness in a short length of combustion tube. The product is carried through a train of well cooled flasks, a

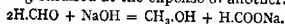
40 per cent. solution of the aldehyde collecting in the first, and weaker solutions in the others. The pure aldehyde is obtained by heating paraformaldehyde, and condensing the vapour in a freezing mixture.

*Formaldehyde*,  $\text{H}\cdot\text{CHO}$  (Hofmann, 1867), is a very pungent and acrid gas which condenses to a liquid at  $-21^\circ$ , and freezes at  $-92^\circ$ . Pure formaldehyde is very unstable, and when warmed even to  $0^\circ$  polymerises explosively with evolution of much heat. The 40 per cent. solution is quite stable, however, and is used as an antiseptic, under the name of *formalin*; on attempting to concentrate further it is gradually converted into a soluble solid polymeride.

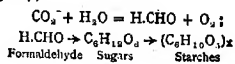
In its general actions formaldehyde closely resembles acetaldehyde; it is readily oxidised to formic acid by mild oxidising agents, and thus reduces silver solutions in the cold; it even reduces hydrogen peroxide to hydrogen in warm alkaline solution. It is reduced to methyl alcohol by sodium amalgam, and vividly colours bleached rosaniline.

Formaldehyde also combines with alcohols; *methylal*,  $\text{H}\cdot\text{CH}(\text{OMe})_2$ , the compound formed with methyl alcohol, is a stable liquid which boils at  $42^\circ$ , and resembles acetal; *ethylal*,  $\text{H}\cdot\text{CH}(\text{OEt})_2$ , boils at  $89^\circ$ . The aldehyde is thus the representative of *dihydroxymethane*,  $\text{H}\cdot\text{CH}(\text{OH})_2$ .

Formaldehyde condenses with hydroxylamine to *formaldoxime*,  $\text{H}\cdot\text{CH}\cdot\text{N}\cdot\text{OH}$ , an unstable liquid which boils at  $85^\circ$ , and is converted into formonitrile on boiling with water. It forms condensation products with phenylhydrazine, and additive compounds with sodium hydrogen sulphite and hydrogen cyanide. It differs from acetaldehyde in its action with ammonia and the alkalis; it neutralises ammonia with development of much heat, owing to the formation of a crystalline condensation product, *hexamethylene-tetramine* or *urotropine*,  $\text{N}_4(\text{CH}_2)_6$ ; and it is converted by dilute caustic alkalis into methyl alcohol and the formate, one molecule of the aldehyde being oxidised at the expense of another.



Formaldehyde polymerises in the same way as its prototype; the *metaformaldehyde* or *trioxymethylene*,  $\text{C}_3\text{H}_6\text{O}_3$ , formed by spontaneous polymerisation, is a soluble crystalline substance which melts at  $171^\circ$ , and is dissociated into the mother substance when vaporised, or heated with water at  $130^\circ$ . Formaldehyde is also directly polymerisable to inactive fructose,  $\text{C}_6\text{H}_{12}\text{O}_6$ , a sugar which is closely connected with the natural sugars. As formaldehyde is probably the initial product in the assimilation of carbon dioxide by living plants, it is a natural synthetic agent of great importance (§ 187).









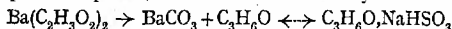
## CHAPTER XVI

### THE KETONES AND SECONDARY ALCOHOLS

**98. Acetone.**—It has been known for several centuries that when sugar of lead is distilled, a volatile inflammable spirit passes over, but it was only in the eighteenth century that this spirit was recognised to be different from alcohol. It is termed acetone.

Acetone is readily made in the laboratory by distilling barium acetate, which has previously been heated on a sand-bath to eliminate water of crystallisation, and reduced to a fine powder; the operation is carried out in the same way as in the preparation of aldehyde (Fig. 17), and at as low a temperature as possible.

The crude product is purified by means of the crystalline bisulphite compound, which it resembles aldehyde in forming.



On shaking the distillate with sodium hydrogen sulphite solution, which is conveniently prepared by saturating warm water with sodium pyrosulphite ("metabisulphite"), much heat is developed, and the mixture rapidly sets to a white crystalline mass of *acetone sodium sulphite*,  $\text{C}_2\text{H}_4\text{O} \cdot \text{NaHSO}_3$ , which is dried on a porous plate. On distilling the bisulphite compound with a concentrated solution of sodium carbonate, acetone passes over, while the sulphurous acid remains behind as normal sodium sulphite; the acetone is finally dried with calcium chloride and redistilled.

Acetone is also formed in considerable quantity in the distillation of hard wood, and is thus present in crude wood spirit. The spirit, after removing the acid and water by distillation with lime, consists of a mixture of acetone and methyl alcohol, which are roughly separable by fractionation.

Crude commercial acetone is obtained either in this way, or by the dry distillation of crude calcium acetate (calcium "pyrolignite"), and the pure substance is prepared from it by the bisulphite method. Acetone is often present in con-

siderable quantities in diabetic urine, in which it is formed by the decomposition of acetoacetic acid (§ 143).

*Acetone*,  $\text{CH}_3\text{CO}\cdot\text{CH}_3$  (Lemery, seventeenth century), is a mobile, inflammable liquid, which has a characteristic ethereal odour; it boils at  $57^\circ$ , freezes at  $-95^\circ$ , and has a specific gravity of 0.812 at  $0^\circ$ . It is freely miscible with water and alcohol, but can be salted out from its aqueous solutions by calcium chloride, and is used as a solvent in organic work.

The molecular formula of acetone is  $\text{C}_3\text{H}_6\text{O}$ , so that it is isomeric with propaldehyde, and is formed by direct resolution of the acetate molecule into two simpler molecules.

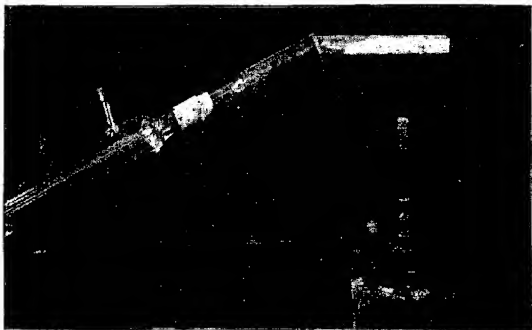
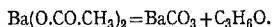


Fig. 17.—Dry or Destructive Distillation.

### 89. Additive Compounds and Condensation Products of Acetone.

—The mode of formation of acetone is analogous to that of the aldehydes from barium formate and the barium salts of the fatty acids, and the resemblance extends in a general manner to its chemical actions.

Acetone is closely allied to the aldehydes; it does not reduce silver nor colour bleached rosaniline, when quite pure, nor does it form polymerides; but in common with the aldehydes it forms various additive compounds and condensation products, and does not interact with acetyl chloride.

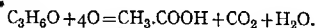
*Acetone sodium hydrogen sulphite*,  $\text{C}_3\text{H}_6\text{O}\cdot\text{NaHSO}_3$  (Limpricht, 1855), is similar to aldehyde sodium sulphite. *Acetone hydrocyanide*,  $\text{C}_3\text{H}_6\text{O}\cdot\text{HCN}$ , resembles aldehyde hydrocyanide, and is converted by acids in a similar

manner into a homologue of lactic acid. An additive compound with ammonia is not known, but several condensation products have been isolated.

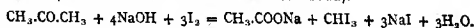
Similarly acetone condenses with hydroxylamine and phenylhydrazine, forming products which are closely akin to the corresponding aldehyde compounds, and are made and decomposed in the same way. *Acetoxime*,  $C_3H_5:N.OH$  (V. Meyer, 1883), is a crystalline solid, which melts at  $69^\circ$ ; *acetone phenylhydrazone*,  $C_3H_5:N.NH.C_6H_5$ , is a liquid of high boiling point, which crystallises to a solid melting at  $16^\circ$ .

Like aldehyde, acetone also condenses with itself. On saturating the liquid with hydrogen chloride gas two products are formed, *mesityl oxide*,  $C_6H_{10}O$ , a liquid of peppermint odour, which boils at  $130^\circ$ , and *phorone*,  $C_8H_{14}O$ , a yellowish crystalline solid which melts at  $28^\circ$  (§ 107). By the further dehydrating action of concentrated sulphuric acid, an aromatic hydrocarbon, *mesitylene*,  $C_9H_{12}$  (§ 328), is formed.

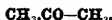
**90. Oxidation of Acetone: its Constitution.**—When acetone is boiled with acid permanganate in a reflux apparatus, carbon dioxide is evolved in abundance, and on distilling the product after the permanganate has ceased to be decolorised, acetic acid passes over.



A similar oxidation is effected in the preparation of chloroform, bromoform and iodoform from acetone, by the action of hypochlorites, etc., the acetyl group being separated as acetic acid, whilst the third carbon atom forms the nucleus of the halogen-methane. The action proceeds at the ordinary temperature, and is quantitative, so that acetone may conveniently be estimated by conversion into iodoform by means of sodium hypoiodite (iodine and caustic or carbonated soda).

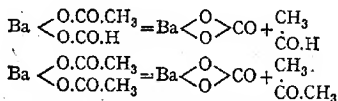


Although isomeric with propaldehyde, acetone thus differs from it in breaking up on oxidation. Since it yields acetic acid, it must certainly contain the group  $CH_3.C\equiv$ , and in all probability the acetyl group; and in this case its molecule must consist of a methyl radical linked to an acetyl radical.



Acetone as Acetyl-methane.

This view is in harmony with its formation from barium acetate, for the action is parallel to the formation of aldehyde from barium acetate and formate (Williamson, 1857).

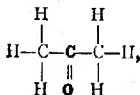


The above constitution is confirmed by the action of phosphorus pentachloride, which converts acetone into *acetone chloride*,  $C_3H_5Cl_2$ , a colourless liquid which resembles ethylidene chloride, but boils at  $70^\circ$ ; the oxygen

of acetone is therefore present as carbonyl, as in the aldehydes, and not as hydroxyl, as in the alcohols, a conclusion which is confirmed by the fact that the compound does not interact with acetyl chloride, or acids.

As hydrogen cannot serve as a link, the remaining carbon atoms are bound to the carbon of the carbonyl group; in other words, the three carbon atoms of the acetone molecule are linked together, and acetone is derived from the hydrocarbon, propane. There are two carbonyl formulae possible for a three-carbon compound of this composition, namely,  $\text{CH}_3\text{CH}_2\text{CO.H}$  and  $\text{CH}_3\text{CO.CH}_3$ ; as the first of these has already been assigned to propaldehyde, the second must be that of acetone.

Acetone is accordingly represented by a structural formula, in which two alkyl groups are linked to a carbonyl radical; when so linked, this radical is known as the ketonic or keto-group.

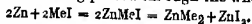


Structural Formula of Acetone; Ketonic Carbonyl.

In the aldehydes the carbonyl is linked only to one alkyl group, and the other valency is satisfied by hydrogen.

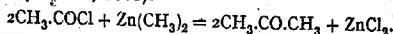
**91. Synthesis of Acetone from Methyl and Acetyl.**—The presence of acetyl and methyl groups in the acetone molecule is independently proved by its synthesis from acetyl chloride and a methyl compound, zinc methyl.

Zinc methyl is made by boiling methyl iodide with a mixture of zinc dust and reduced copper; the reflux apparatus, which is heated on a water bath, is provided with a mercury valve, so that the air may be replaced by dry carbon dioxide before the action is commenced, as the product is very oxidisable. When methyl iodide ceases to run back from the condenser the solid product is distilled from an oil-bath at  $160^\circ$  and upwards, a stream of carbon dioxide being passed through the whole apparatus.

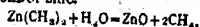


*Zinc methyl*,  $\text{ZnMe}_2$  (Frankland, 1852), is a colourless liquid, which is spontaneously inflammable in air, and must be kept in sealed vessels; it boils at  $46^\circ$ , freezes at  $-40^\circ$ , and has a specific gravity of 1.386 at  $10^\circ$ .

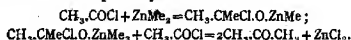
When it is mixed with acetyl chloride, a violent action occurs, and on distilling the solid product of the action with water, the chlorine is exchanged for methyl and acetone is generated (Freund, 1861).



The molecular formula of zinc methyl calculated from its vapour density is  $\text{ZnC}_2\text{H}_6$ , and as the compound is hydrolysed by water quantitatively to zinc oxide and methane, its molecule contains two methyl groups linked to an atom of zinc.

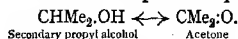


Zinc methyl is of great use in synthesis, as it affords a means of exchanging methyl for halogen. The mechanism of the action is not quite as simple, however, as would at first sight appear; the crystalline compound obtained in the first instance in the above synthesis is formed by direct combination of the acetyl chloride with the zinc methyl, and interacts with a further quantity of the chloride.



**92. Reduction of Acetone to Secondary Propyl Alcohol: Position Isomerism.**—On reducing acetone with sodium amalgam in acid solution, a compound is obtained (Friedel, 1862), which has the same composition and vapour density as propyl alcohol. It is an alcohol, as it forms a sodium derivative, and is converted into an acetate by acetyl chloride; but its boiling point and specific gravity are lower than those of ordinary propyl alcohol, with which it is isomeric.

When this secondary propyl alcohol is boiled with chromic acid mixture, acetone is re-formed, and may be isolated and identified by means of its bisulphite compound (Friedel, 1863).



We have seen that the higher alcohols may be regarded as alkyl substitution products of methyl alcohol, in which a hydrogen atom of the methyl group is replaced by an alkyl radical. They may therefore be termed alkyl-methyl alcohols; ordinary alcohol is then methyl-methyl alcohol,  $\text{CH}_3\text{Me.OH}$ . It follows logically from this nomenclature that there should be more complex alcohols, such as dimethyl-methyl alcohol,  $\text{CHMe}_2\text{OH}$ , and trimethyl-methyl alcohol,  $\text{CMe}_3\text{OH}$  (Kolbe, 1858).\*

If the alcohol obtained by reducing acetone, is the isomeride of propyl alcohol required by the above considerations, it should be reconverted by oxidising agents, not into an aldehyde and an acid containing the same number of carbon atoms, as is the case with the ordinary alcohols, but into acetone or the oxidation products of this substance (Kolbe, 1862); this requirement is fulfilled by the above experimental result.

When the reduction of acetone is effected by means of sodium in alkaline solution, it is arrested mainly at an intermediate stage, and a complex ditertiary alcohol (§ 98), pinacone, is formed. *Pinacone* or *tetramethylglycol*,  $\text{CMe}_2(\text{OH}).\text{CMe}_2(\text{OH})$  (compare § 120), is a crystalline substance melting at  $38^\circ$ ; like isopropyl alcohol it is re-oxidised to acetone by chromic acid mixture, and converted into isopropyl iodide by gaseous hydriodic acid. When boiled with dilute sulphuric acid it is converted by a curious transformation into *pinacolin* or *trimethylacetone*,  $\text{CMe}_3\text{CO.CH}_3$ , a liquid of peppermint odour, boiling at  $106^\circ$ .

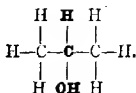
*Secondary propyl (isopropyl) alcohol*,  $\text{CHMe}_2\text{OH}$  (Berthe-

\* If methyl alcohol be termed *carbinol*, these alcohols become *dimethylcarbinol* and *trimethylcarbinol* respectively (Kolbe).

lot, 1855), is a liquid which closely resembles normal propyl alcohol (§ 45), but boils at  $82^{\circ}$ , and has a specific gravity of 0.792 at  $15^{\circ}$ ; it constitutes about 15 per cent. of fusel oil.

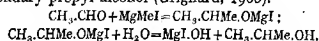
Secondary propyl alcohol was first obtained by hydrolysis of the propyl hydrogen sulphate formed from propylene (§ 106), and was thought at the time to be the analogue of ordinary alcohol required by the rule of homology.

The structural formula of this alcohol follows from its interconvertibility with acetone.



Structural Formula of Secondary Propyl Alcohol.

The structure is further confirmed by synthesis of the alcohol from acetaldehyde and magnesium methiodide. As already stated, magnesium turnings dissolve with great energy in a solution of methyl iodide in dry ether, and if pure acetaldehyde be added to the ethereal solution of magnesium methiodide, a crystalline additive product is obtained, from which, after the ether has been removed by distillation, dilute sulphuric acid liberates secondary propyl alcohol (Grignard, 1900).



**93. The Secondary Propyl Compounds.**—Secondary propyl alcohol forms a series of esters, etc., which are distinct from the corresponding propyl compounds. The most important of these is the iodide; it is best prepared by repeatedly distilling diluted glycerol with iodine and yellow phosphorus, or by boiling glycerol with concentrated hydriodic acid in a reflux apparatus (§ 131).

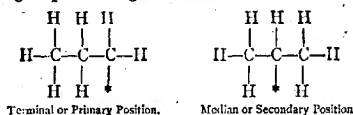
*Secondary propyl (isopropyl) iodide*,  $\text{CH}_3\text{CHI.CH}_3$  (Berthelot, 1857), is a heavy, colourless liquid, which resembles ethyl and normal propyl iodides, but boils at  $90^{\circ}$ .

Secondary propyl iodide is converted by caustic alkalies, not into the alcohol, but into its dehydration product, propylene, and this is the case with most of the iodides higher than ethyl iodide. When boiled with lead oxide and water, however, it is readily hydrolysed, and the same transformation can be effected by heating it with silver acetate, and then hydrolysing the isopropyl acetate in the ordinary way.

When secondary propyl iodide is heated with silver oxide it is converted into *secondary propyl ether*,  $(\text{CHMe})_2\text{O}$ , a liquid of peppermint odour, which boils at  $82^{\circ}$ , but resembles ordinary ether in its actions.

The secondary propyl compounds are thus the derivatives of an alkyl radical, secondary propyl (isopropyl),  $\text{CHMe}_2$ , or  $\text{Pr}^2$ , which is isomeric with and analogous in

function to the ordinary or primary propyl radical. The isomerism of the propyl and secondary propyl compounds, and of propaldehyde and acetone, is termed *position isomerism*, as it depends on the variation in the position of the active group with regard to the carbon chain.



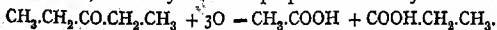
Both sets of compounds are derived from propane, but whilst the substituent group in the primary propyl compounds is attached to a carbon atom, to which only one other carbon atom is united, in the secondary propyl compounds this carbon atom is directly linked to two others.

**94. The Ketones and Secondary Alcohols.**—By distilling the homologues of barium acetate, or acting on the acid chlorides with the respective zinc alkyls, compounds are formed which are homologous with and analogous to acetone. They are termed on this account, *ketones*.\* The ketones may also be named after their constituent alkyl radicals or parent hydrocarbons; acetone is *dimethyl ketone* or *ketopropane*, and propione, which is derived similarly from propionic acid, is *diethyl ketone* or  *$\beta$ -ketopentane*.

*Propione*,  $\text{C}_2\text{H}_5\cdot\text{CO}\cdot\text{C}_2\text{H}_5$ , a pleasant-smelling liquid, boiling at  $103^\circ$ , is formed from barium propionate; *butyrone*,  $\text{C}_3\text{H}_7\cdot\text{CO}\cdot\text{C}_3\text{H}_7$ , a similar liquid, boiling at  $144^\circ$ , is formed by distilling barium butyrate.



In their action with oxidising agents the ketones resemble their prototype, and yield acids whose molecules contain fewer carbon atoms; propione is resolved into acetic and propionic acids, and butyrone into propionic and butyric acids.



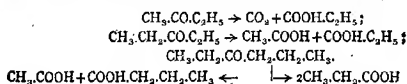
By distilling mixtures of barium salts, mixed ketones are obtained, the formation of which suggested the preparation of aldehydes by the barium formate method (Williamson, 1851). *Methyl ethyl ketone*,  $\text{CH}_3\cdot\text{CO}\cdot\text{C}_2\text{H}_5$ , obtained from barium acetate and propionate, is a liquid boiling at  $81^\circ$ ; *methyl n-propyl ketone*,  $\text{CH}_3\cdot\text{CO}\cdot\text{CH}_2\text{Et}$ , from barium acetate and butyrate, boils at  $104^\circ$ , and *ethyl n-propyl ketone*,  $\text{C}_2\text{H}_5\cdot\text{CO}\cdot\text{CH}_2\text{Et}$ , from barium propionate and butyrate, boils at  $123^\circ$ .

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*German Ketone, from French actions.*

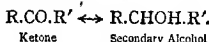


In the oxidation of the ketones, the molecule is broken between the carbonyl and one of the alkyl groups, because oxidising agents always attack that part which already contains oxygen or other electronegative element. Methyl ethyl ketone yields carbon dioxide and acetic and propionic acids, when oxidised with chromic acid mixture, just as diethyl ketone gives propionic and acetic acids; whilst *ethyl propyl ketone* is resolved into acetic, propionic and butyric acids.

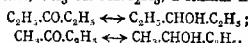


The ketones condense with hydroxylamine and phenylhydrazine in precisely the same way as acetone, and the compounds thus formed are useful in isolating and characterising them. The hydroxylamine compounds are known as ketoximes; it is only those ketones which contain a methyl group that form crystalline bisulphite compounds, but most of them unite with hydrocyanic acid, and several important syntheses have been effected by means of this reaction; that of citric acid (§ 165) may be mentioned.

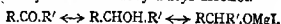
When reduced with sodium amalgam, best in moist ethereal solution, the ketones are converted into alcohols, which bear the same relation to secondary propyl alcohol as the ordinary alcohols to normal propyl alcohol. There is one of these secondary alcohols for every ketone, just as there is an ordinary alcohol for every aldehyde.



Propione is reducible to *secondary amyl alcohol*,  $\text{C}_5\text{H}_{11}\cdot\text{CHOH}\cdot\text{C}_2\text{H}_5$ , a liquid of fusel odour, boiling at  $117^\circ$ , and methyl ethyl ketone yields *secondary butyl alcohol*,  $\text{CH}_3\cdot\text{CHOH}\cdot\text{C}_2\text{H}_5$ , a similar liquid boiling at  $100^\circ$ .



Many of these secondary alcohols have also been formed synthetically from lower aldehydes by the magnesium alkyl-iodide method (§ 92); propionic aldehyde thus yields secondary butyl alcohol.



The ordinary alcohols, in which only one of the methyl hydrogen atoms is replaced by alkyl, are termed *primary alcohols*, and are distinguished by the presence of the primary alcohol group.



The Primary Alcohol Group.

The isomeric alcohols, homologous with secondary propyl alcohol, in which two of the methyl hydrogen atoms are replaced, are termed *secondary alcohols*, and are

characterised by the presence of the secondary alcohol group.

**:CHOH.**

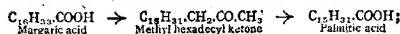
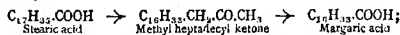
The Secondary Alcohol Group.

Like their prototype, the secondary alcohols are reconverted into ketones by gentle oxidation, and are broken up by more powerful oxidising agents. With this exception they resemble the ordinary alcohols, and form salts with acids in the same way; the boiling points of the secondary alkyl compounds are somewhat lower than those of their primary isomerides.

The normality of the higher paraffins and their derivatives has been established by a process of degradation, connecting them, through the related methyl ketones, with capric acid (§§ 45, 81), the normal constitution of which has been established synthetically (§ 145).

Calcium stearate is converted by distillation with calcium acetate into *methyl heptadecyl ketone*, which is then oxidised by chromic acid mixture to acetic acid and margaric acid (§ 81). Margaric acid is converted similarly into *methyl hexadecyl ketone* and palmitic acid; palmitic acid into pentadecic acid (§ 81); and so on, step by step, until the ten-carbon normal acid is reached.

As these higher acids and ketones are reducible to the corresponding paraffins by the hydriodic acid method (§ 78), the latter are also normal (Krafft, 1882).



**95. Synopsis.**—The ketones are compounds which are isomeric with the aldehydes. They differ from these in that they are oxidisable to acids containing fewer carbon atoms in the molecule, and are reducible to secondary alcohols which are isomeric with the ordinary or primary alcohols. They contain the ketonic group CO linked to two alkyl groups, and the secondary alcohols contain the characteristic group CHOH, similarly linked.



## CHAPTER XVII

### THE FOUR BUTYL ALCOHOLS AND THEIR HOMOLOGUES

**96. Normal and Secondary Butyl Alcohols.**—Whilst only one methyl alcohol and one ethyl alcohol are known, there are two propyl alcohols, and as the number of carbon atoms increases, the isomerism of the alcohols rapidly becomes very complicated. There are four butyl alcohols, and no fewer than eight amyl alcohols.

The butyl alcohol corresponding with ordinary butyric acid does not occur in nature, and is prepared synthetically from the acid, through the corresponding aldehyde.

The aldehyde formed by distilling a mixture of calcium butyrate and formate is converted into the alcohol by reduction with sodium amalgam in moist ethereal solution, and the alcohol is isolated from the product by successive conversion into the iodide and acetate, in the manner described under isopropyl alcohol.

*Primary or normal butyl alcohol*,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$  (Lieben and Rossi, 1869), is a liquid of slightly fusel odour, boiling at  $117^\circ$ . When gently oxidised it is reconverted into butaldehyde and butyric acid, an acid containing the same number of carbon atoms in the molecule; it is therefore a primary alcohol like *n*-propyl alcohol, and contains the primary alcohol group,  $\text{CH}_2\text{OH}$ .



Secondary butyl alcohol, like secondary propyl alcohol, can be prepared by reducing the corresponding ketone, namely methyl ethyl ketone, with sodium amalgam (Friedel, 1869).

It was first obtained from secondary butyl hydrogen sulphate and butylene (§ 106), in the same way as secondary propyl alcohol from propylene, and may also be made from secondary butyl iodide and erythritol (§ 188), in the same way as secondary propyl alcohol from glycerol.

*Secondary butyl alcohol*,  $\text{CH}_3\text{CH}_2\text{CHOHCH}_3$  (De Luynes, 1863), is a liquid boiling at  $100^\circ$ . It forms the usual alcoholic



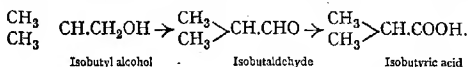
of butyric odour, boiling at  $154^{\circ}$ . Unlike butyric acid it is only sparingly soluble in water, from which it may be salted out by sodium chloride; its calcium salt, unlike calcium butyrate, is more soluble in hot than in cold water.

Finally it is oxidised by chromic acid to carbon dioxide and acetic acid, whereas normal butyric acid is practically unaffected. The dissociation constant of isobutyric acid,  $K=0.0014$ , is nearly identical with that of *n*-butyric acid.

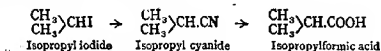
The corresponding aldehyde, *isobutaldehyde*,  $\begin{smallmatrix} \text{CH}_3 \\ | \\ \text{CH}_3 \end{smallmatrix} \text{CH} \cdot \text{CHO}$ , a liquid boiling at  $64^{\circ}$ , may be obtained in the customary manner, either by distilling the calcium salt of the acid with calcium formate, or by cautiously oxidising the alcohol with dilute chromic acid mixture. It is quite distinct from butaldehyde, which boils at  $74^{\circ}$ ; and is reconverted into isobutyl alcohol by reduction with sodium amalgam.

As isobutyl alcohol is converted by oxidising agents into an acid containing the same number of carbon atoms, it is a primary alcohol, and contains the primary alcohol group,  $\text{CH}_2\text{OH}$ . Similarly isobutyric acid, as a typical acid contains the carboxyl or acid group,  $\text{COOH}$ . The difference therefore lies in the propyl radical.

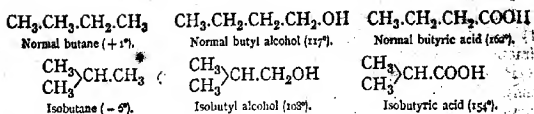
Normal butyric acid is proved by the cyanide synthesis to be propyl-formic acid,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{COOH}$  (§ 64), so that *n*-butyl alcohol is propyl-methyl alcohol,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$ ; and as there are only two sets of propyl compounds, isobutyl alcohol must be an isopropyl derivative (§ 92).



There is no other possibility of isomerism, and isobutyric acid should therefore be formed by the cyanide synthesis from isopropyl alcohol, in the same way as ordinary butyric acid from normal propyl alcohol. As a matter of fact, the nitrile which is obtained on boiling isopropyl iodide with alcoholic potassium cyanide, is identical with *isobutyronitrile*, and yields on hydrolysis an acid, identical with the isobutyric acid from fusel oil (Erlenmeyer, 1867; compare § 145).

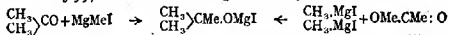


Isobutyl alcohol and isobutyric acid are derivatives of isobutane, and are branching-chain compounds. It is noteworthy that the branching of the chain is associated with lowering of the boiling-point, as shown in the following table.



88. **Tertiary Butyl Alcohol.**—The existence of the fourth butyl alcohol was foreshadowed by the same reasoning which led to the recognition of the secondary alcohols (Kolbe, 1860; § 92). The primary and secondary alcohols being mono- and di-alkyl-derivatives of methyl alcohol (§ 92), there should be tri-alkyl-derivatives or tertiary alcohols, of which the simplest must be trimethyl-methyl or tertiary-butyl alcohol,  $\text{CMe}_3\text{OH}$ .

Tertiary butyl alcohol can be made from acetyl chloride and zinc methyl by a modification of the acetone synthesis (§ 91), but is best prepared by the magnesium-alkyl synthesis (§ 92). Dry acetone (1 mol.) or methyl acetate ( $\frac{1}{2}$  mol.) is added to an ethereal solution of magnesium methiodide (1 mol.), and an additive compound is formed from which tertiary butyl alcohol is set free by dilute sulphuric acid (Grignard, 1900; see also § 99). The alcohol is purified by fractionation.



**Tertiary-butyl alcohol**,  $\text{CMe}_3\text{OH}$  (Butlerow, 1862), is a crystalline solid resembling camphor in odour; it melts at 25°, and boils at 83°, and is thus more volatile and more easily solidified than its isomerides with longer carbon chains.

Tertiary-butyl alcohol forms a *sodium derivative*, and an *acetate, isoxide*, etc., so that its alcoholic nature is undoubted, but when oxidised with chromic acid mixture it breaks up altogether, yielding carbon dioxide and acetone, together with acetic acid from the oxidation of the latter. As no acid or ketone containing the same number of carbon atoms can be isolated from the product, the alcohol is neither a primary nor a secondary alcohol.

Theory indicates that it is a trimethyl-derivative of methyl alcohol, and the synthesis from acetone fully confirms this view. Tertiary butyl alcohol therefore contains the tertiary alcohol group.



Tertiary Alcohol Group.

The tertiary butyl radical,  $\text{CMe}_3$ , bears the same relation to the isobutyl radical,  $\text{CH}_2\text{CHMe}_2$ , as the secondary butyl radical,  $\text{CHMeEt}$ , to the normal radical,  $\text{CH}_2\text{CH}_2\text{Et}$ .

89. **The Amyl Alcohols and Valeric Acids.**—As the two propyl alcohols give rise to four butyl alcohols and two butyric acids, it may be expected that the four butyl alcohols will give rise to a still larger number of amyl alcohols and valeric acids. There are in fact four primary amyl alcohols, and therefore four valeric acids, and in addition to these there are three secondary amyl alcohols, and one tertiary amyl alcohol.

**Normal amyl alcohol**,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$ , and **normal valeric acid**,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$ , do not occur in nature, and are prepared synthetically from normal butyl alcohol by the cyanide method (Lieben and Rossi, 1871).

\* This group should be carefully distinguished from the aldehyde group  $\text{CHO}$ , in which the carbon atom is linked to only one other carbon atom.

The chief amyl alcohols are two primary alcohols occurring in fusel oil (§ 45), of which they constitute about one-third by volume. The main fraction obtained from dry potato-spirit oil boils fairly constantly at 130–132°, and was long thought to be a chemical individual, and termed amyl alcohol (Dumas, *amylum* = starch). But the specific rotatory power of this alcohol varies with different specimens, and as the rotatory power of a pure substance (§ 139), like any other property, is constant, it follows that the fusel alcohol is a mixture.

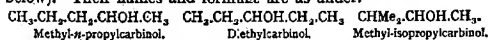
Commercial amyl alcohol is resolved into its two constituents by fractionally crystallising barium amyl sulphate from water. The less soluble salt yields on hydrolysis an alcohol, which is optically inactive, whilst the alcohol from the more soluble active salt remaining in the mother-liquor has a constant rotatory power (Pasteur, 1855).

*Fermentation, inactive or isoamyl alcohol*,  $\text{CHMe}_2\text{CH}_2\text{CH}_2\text{OH}$ , which constitutes about 25 per cent. of potato fusel oil, is a liquid of rank, penetrating odour, which boils at 131°. Its constitution follows from its oxidation to the corresponding acid. *Isovaleric acid*,  $\text{CHMe}_2\text{CH}_2\text{COOH}$ , is an oily liquid of very clinging and unpleasant odour, which occurs naturally in the root of the lesser valerian; it boils at 175°. The constitution of isovaleric acid as an isobutyl derivative follows from its synthesis from isobutyl alcohol by the cyanide method (Erlenmeyer, 1870).

*Active amyl alcohol*,  $\text{CHMeEtCH}_2\text{OH}$ , is an optically active, but otherwise similar liquid, boiling at 131°; its constitution follows from its oxidation to the corresponding valeric acid. *Active valeric acid*,  $\text{CHMeEtCOOH}$ , is an oily liquid, boiling at 177°, and its constitution as methyl-ethyl-acetic acid is proved by its synthesis from acetic acid by the aceto-acetic method (§ 145).

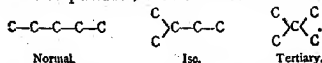
The fourth primary amyl alcohol and corresponding valeric acid are derived from tertiary butyl alcohol. *Trimethylacetic acid*,  $\text{CMe}_3\text{COOH}$ , a crystalline substance, which resembles acetic acid in odour, is made from tertiary butyl iodide by the cyanide synthesis; it is also formed by oxidising trimethylacetone (§ 92) with chromic acid mixture. *Trimethylcarbinol*,  $\text{CMe}_3\text{CH}_2\text{OH}$ , is a crystalline substance, which is formed by reducing the acid chloride with sodium amalgam.

The secondary amyl alcohols, which are all liquid substances, can be made by reducing the corresponding ketones (§ 94), and in other ways (see below). Their names and formulae are as under.



*Tertiary-amyl alcohol*,  $\text{CMe}_2\text{EtOH}$ , is a liquid of camphor odour, boiling at 102°. It is formed from propionyl chloride and zinc methyl, or from methyl ethyl ketone or ethyl propionate, and magnesium methiodide, in an analogous manner to tertiary butyl alcohol.

The amyl alcohols and their derivatives are thus substitution products of the three pentanes, built on three distinct nuclei.



Normal

Iso.

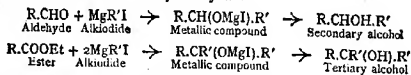
Tertiary.

As the series is ascended, and the possibilities of branching become greater, it is obvious that the isomerism must become very complex. There should be eight primary, six secondary, and three tertiary hexyl alcohols, and these fourteen have been prepared. Thirteen of the heptyl alcohols, and nine of the octyl alcohols are known, and there is no



doubt that very many more could be made. Above this point the isomerism of the alcohols has been little investigated.

A very convenient method of preparing the complex higher alcohols is afforded by the magnesium alkyl synthesis (Grignard), the secondary alcohols being made from the aldehydes (§ 92), and the tertiary alcohols from the ketones or esters (§ 98). Such compounds as *dimethyl-n-propyl-carbinol* (tertiary hexyl alcohol),  $\text{CMePr}_2\text{OH}$ , b.p.  $124^\circ$ , and the corresponding *diethyl compound* (tertiary octyl alcohol), b.p.  $159^\circ$ , have been made in this manner from ethyl butyrate.



**100. Synopsis.**—In addition to the primary and secondary butyl alcohols analogous to propyl and isopropyl alcohol, there are two more, together with a related acid, derived from isopropyl alcohol, and built on a branching chain carbon nucleus. All alcohols are either primary, secondary, or tertiary derivatives of methyl alcohol. The primary alcohols are oxidisable to aldehydes and acids containing the same number of carbon atoms, the secondary alcohols to ketones, whilst the tertiary alcohols break up when oxidised.



## CHAPTER XVIII

### THE HYDROCARBONS AS THE BASIS OF CLASSIFICATION

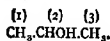
101. *The Hydrocarbons as the Basis of Classification.*—The paraffins form a very valuable link between the various classes of compounds. The isomerism of the butyl and amyl alcohols, although accounted for by their relation to methyl alcohol, is much more concisely expressed by reference to the position of the hydroxyl group in the two butane and three pentane chains (§ 80). The modern system of classification is based on this principle, the alcohols and their derivatives being regarded as substitution products of the related hydrocarbons (§§ 75, 77).

Methyl alcohol,  $\text{CH}_3\text{OH}$ , is *hydroxy-methane*; ethyl alcohol,  $\text{CH}_3\text{CH}_2\text{OH}$ , is *hydroxy-ethane*; normal propyl alcohol,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$ , is  $\alpha$ -*hydroxy-propane*; and isopropyl alcohol,  $\text{CH}_3\text{CHOHCH}_3$ , is  $\beta$ -*hydroxy-propane*. The four butyl alcohols are respectively  $\alpha$ - and  $\beta$ -*hydroxy-butane*, and  $\alpha$ - and  $\beta$ -*hydroxy-isobutane*. Acetone may be termed *keto-propane*, and the two normal five-carbon ketones respectively  $\alpha$ - and  $\beta$ -*keto-pentane*.

The operations involved in converting the natural paraffins into any of their derivatives are difficult and tedious (compare Benzene), but this does not lessen the value of the system, which lies in referring all types of compounds to the simplest.

102. *International Nomenclature.*—To provide names for all classes of compounds on this plan, an International system of nomenclature has been devised (Geneva Conference, 1892), in which the stems of the names represent the parent hydrocarbons, and the substituted groups are indicated by suffixes or prefixes. Alcohol is *ethanol*; aldehyde is *ethanal*; acetic acid is *ethanoic acid*; and ethyl chloride is *chloroethane*.

Position isomerides, such as the propyl alcohols, are distinguished by numerical prefixes. Normal propyl alcohol is *1-propanol*, and its isomeride *2-propanol*, the carbon atoms being numbered from the end of the chain—



The ketones are distinguished by the suffix *one*. Acetone,  $\text{CH}_3\text{COCH}_3$ , is *propanone*; propione,  $\text{CH}_3\text{CH}_2\text{COCH}_2\text{CH}_3$ , is *3-pentanone*; whilst the metameric methyl-propylketone,  $\text{CH}_3\text{COCH}_2\text{CH}_2\text{CH}_3$ , is *2-pentanone*.

The chain isomerism of the butanes and their derivatives is indicated in a similar manner, the branching chain compounds being classed as alkyl derivatives of the longest carbon chain in the molecule. Isobutane is *2-methyl-propane*,  $\text{CH}_3\text{CHMeCH}_3$ ; isobutyl alcohol is *2-methyl-1-*

propanol,  $\text{CH}_3\text{CHMeCH}_2\text{OH}$ ; and isobutyric acid,  $\text{CH}_3\text{CHMeCOOH}$ , is *2-methyl-propanoic acid*. Tertiary butyl alcohol is *2-methyl-2-propanol*,  $\text{CH}_3\text{CMeOHCH}_3$ .

The amides, nitriles, and amines also take their names from the related hydrocarbons. Acetamide is *ethanamide*, acetonitrile is *ethane-nitrile*, and ethylamine is *aminoethane*.

102a. *Application of Geneva Nomenclature to Complex Substitution Products.\**—The international nomenclature is convenient in its application to the more complex aliphatic compounds, as it provides names which at once indicate the chemical structure, and thus, to a large extent, the properties of the substance.

Whilst the chloroacetic acids merely become *chloroethanoic acids*, chloral is *trichloroethanal*, and butyl chloral, *2-2-3-trichlorobutanal*. Glycol with its aldehyde and acid become *ethanediol*, *ethanolal*, and *ethanoic acid*; glyoxal and glyoxylic acid are *ethanedial* and *ethanoic acid*; whilst oxalic acid is *ethanedioic acid*.

Glycerol is *1-2-3-propanetriol*; glycerose, *propanediolal*, and glyceric acid, *propane-2-3-dioic acid*. Allyl alcohol with its aldehyde and acid are *1-propenol*, *propenal* and *propenoic acid*, whilst the compounds of the propargyl group are similarly derived from *propyne*.

The lactic acids are respectively *2-propanoic acid* and *3-propanoic acid*, and acetoacetic acid is *3-butanonic acid*.

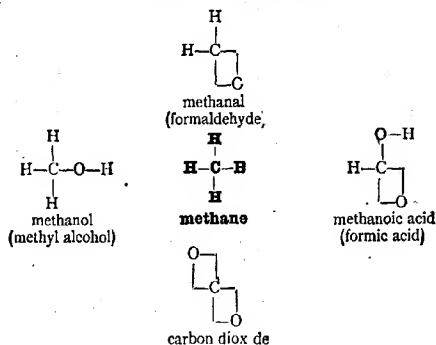
Malonic and succinic acids are *propanedioic acid* and *butanedioic acids*, maleic and fumaric acids being the corresponding *butenedioic compounds*. Malic and tartaric acids become *butanoldioic acid* and *butanedioldioic acids*.

Glucose is *hexanepentolal*, whilst mannitol and sorbitol are *hexanehexols*, and fructose, *hexanepentolone*.

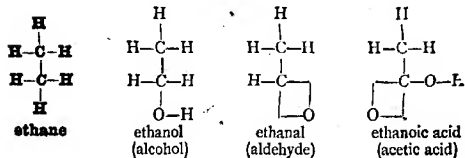
\* The reading of this section should be deferred until these complex substitution products have been studied; it is placed here for convenience.

## THE HYDROCARBONS AS THE BASIS OF CLASSIFICATION.

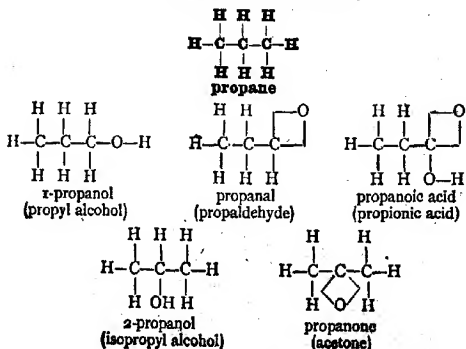
## I. DERIVATIVES OF METHANE.



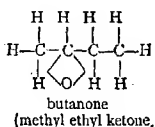
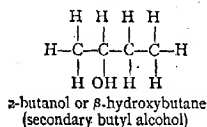
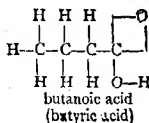
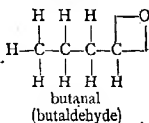
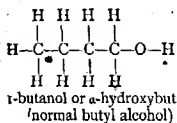
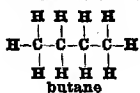
## II. DERIVATIVES OF ETHANE.



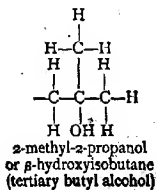
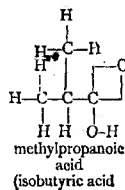
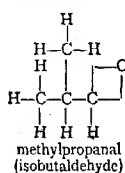
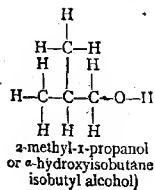
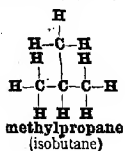
## III. DERIVATIVES OF PROPANE.



IV. DERIVATIVES OF BUTANE.



V. DERIVATIVES OF ISOBUTANE.



## SECTION V

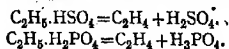
### THE UNSATURATED HYDROCARBONS.

#### CHAPTER XIX<sup>1</sup>

##### THE OLEFINES

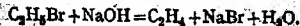
**103. Ethylene.**—Before proceeding to the more complex aliphatic compounds, we must consider two series of hydrocarbons, the olefines and acetylenes, which are closely related to the paraffins, although very different in properties.

Ethylene, the first of the olefines, is usually made by heating alcohol with concentrated sulphuric acid at 180° (Deiman, 1795), but as sulphuric acid chars and oxidises organic matter at this temperature, producing much sulphur dioxide and carbon dioxide, it is better to use orthophosphoric acid (Newth, 1901). The initial product is the acid ester (§§ 25, 26), which at the high temperature is soon decomposed.



Syrupy phosphoric acid is boiled down in a small distilling flask until its temperature reaches 200°, when alcohol is slowly added as in preparing ether (§ 26), the temperature being maintained at 200–220°. Ethylene is rapidly evolved, and once the alcohol supply is adjusted, the action continues for days, the acid remaining unchanged. The gas is separated from alcohol and ether vapours by cooling to 0°, or washing successively with water and concentrated sulphuric acid.

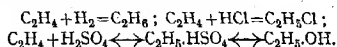
Ethylene is similarly formed when ethyl bromide or iodide is boiled with alcoholic potash, the haloid losing its halogen, instead of exchanging it for hydroxyl as in the action with aqueous potash. The halogen acid is also readily withdrawn by passing the vapour of the halide over red-hot soda-lime.



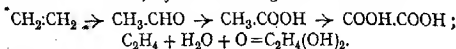
*Ethylene* or *olefiant gas*,  $\text{CH}_2\text{:CH}_2$  (Deiman, 1795), is a colour-

less, insoluble gas, having a sweet odour and taste; the liquefied gas boils at  $-103^{\circ}$ , freezes at  $-165^{\circ}$ , and has a specific gravity of 0.61.

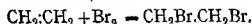
**104. Additive Compounds of Ethylene.**—Whilst the paraffins act only by substitution, and do not even form molecular compounds, the olefines, of which ethylene is the type, form many additive combinations. Ethylene combines directly with hydrogen, when passed with it over reduced nickel at  $140-150^{\circ}$  (Sabatier, 1897), and is thus converted into ethane; it forms ethyl chloride when mixed with hydrogen chloride gas, and ethyl iodide when passed into fuming hydriodic acid: it is rapidly absorbed by concentrated sulphuric acid at  $170^{\circ}$ , or by the fuming acid at ordinary temperatures, forming ethyl hydrogen sulphate, and in this way is easily reconverted into alcohol (Hennell, 1826).



Ethylene is much more easily oxidised than the paraffins; it is converted into aldehyde, acetic acid and oxalic acid when shaken with chromic acid mixture, and into glycol (§ 120) by cold alkaline permanganate. The latter interaction affords a very characteristic test for ethylene and its numerous derivatives (Baeyer, 1894). The compound is shaken with dilute potassium permanganate made alkaline with sodium carbonate, and the permanganate is instantly decolorised with separation of brown, hydrated manganese dioxide.



A most characteristic action of ethylene is its direct combination with halogens. When shaken with bromine water, the bromine is at once decolorised, the solution acquiring a sweet odour like that of chloroform; the additive product to which this odour is due is readily prepared in quantity.



Purified ethylene is passed into bromine beneath a layer of water, in a large flask which is occasionally well shaken; heat is evolved, and the bromine is gradually converted into a heavy, colourless liquid; this is purified by shaking successively with dilute alkali and water, and is dried with calcium chloride before rectification.

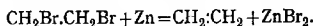
*Ethylene bromide*,  $\text{CH}_2\text{Br.CH}_2\text{Br}$  (Balard, 1827), is a liquid resembling chloroform; it boils at  $132^{\circ}$ , freezes at  $9^{\circ}$ , and has



a specific gravity of 2.19. *Ethylene chloride*,  $\text{CH}_2\text{Cl}.\text{CH}_2\text{Cl}$  (Deiman, 1795), the first compound of this class prepared, is a similar liquid, boiling at  $84^\circ$ , which collects in oily drops (Dutch liquid), when its constituent gases are mixed in a large flask; hence the name *olefiant gas*.

The molecular formulæ of these halogen compounds not only follow from the vapour densities, but can also be deduced from considerations of valency. If the molecular formula of ethylene were  $\text{CH}_2$ , that of the saturated bromide would be  $\text{CH}_2\text{Br}_2$ , or carbon would not be quadrivalent. But this formula does not agree with the analysis, and that of the hydrocarbon must therefore be at least  $\text{C}_2\text{H}_4$ ; for the same reason it cannot be greater than this.

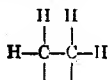
Ethylene bromide and chloride are formed by the direct addition of bromine to the hydrocarbon, and are additive compounds, like aldehyde-ammonia. The ethylene behaves as a bivalent radical, and combines with the halogen in the same way as a bivalent metal such as mercury. Conversely, when ethylene bromide vapour is passed over hot zinc dust, it is reconverted into the hydrocarbon, just as mercury is expelled from its salts by more positive metals.



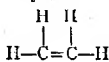
**105. Constitution of Ethylene: Saturated and Unsaturated Compounds.**—Ethylene bromide is isomeric with the ethylidene bromide, which is formed by the action of phosphorus pentabromide on aldehyde. According to the structural formula of ethane (§ 77), there should be two dibrom-ethanes,  $\text{C}_2\text{H}_4\text{Br}_2$ , of the constitution  $\text{CH}_3.\text{CHBr}_2$  and  $\text{CH}_2\text{Br}.\text{CH}_2\text{Br}$ ; as the first of these represents ethylidene bromide (§ 84), the second must represent ethylene bromide.

Compounds such as ethylene and aldehyde, which combine directly with others, are termed unsaturated compounds, and are sharply distinguished from saturated compounds such as ethane and alcohol, from which one or more subsidiary atoms must be displaced before action can occur.

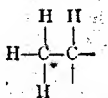
Several structural formulæ can be devised representing this unsaturated character of ethylene:



Free Valences  
Symmetrical



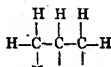
Double Linkage  
Symmetrical



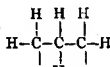
Free Valences  
Unsymmetrical

but a study of its homologues shows that only one of these is available, namely the second, symmetrical formula.

There is only one methyl-ethylene and one ethyl-ethylene (§ 106), whereas, according to the third, unsymmetrical formula, there should be two sets of such derivatives. The first formula with free valencies cannot be adopted, for methyl-ethylene should then exist in two isomeric forms—



Unsymmetrical.

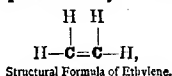


Symmetrical.

the formulae of which would differ in the positions of the free unsaturated valencies; but only one propylene is known.

There is also abundant evidence that in the compounds formed by the addition of bromine to the homologues and analogues of ethylene, the bromine is always added to adjacent carbon atoms (compare § 120). Unsaturated carbon atoms occur almost invariably in pairs; there is never an odd number of such atoms in a hydrocarbon molecule.

Ethylene is thus represented by a formula

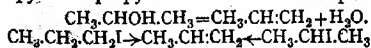


in which the carbon atoms are connected by a double linkage.

The apparent paradox that molecules containing a double linkage are less stable than those containing only a single linkage is discussed later (§ 288). The ready oxidability of ethylene is primarily due to the ease with which it forms additive products. With acid oxidisers, which usually act also as hydrating agents, the initial product is probably alcohol, which is converted into aldehyde, acid, etc., according to the energy of the oxidation. Similarly glycol (§ 120) into which ethylene is converted by cold, dilute alkaline permanganate, is rapidly oxidised to oxalic acid by the same agent at a higher temperature and in a more concentrated form.

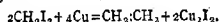
The instability towards oxidising agents of molecules containing the double linkage is thus the direct result of the tendency of this linkage to revert to the single form (§ 288).

**106. The Olefines.**—The first homologue of ethylene is methyl-ethylene or propylene: Propylene is made in the same way as ethylene, but both from propyl and from isopropyl compounds. It is conveniently prepared by boiling a saturated solution of zinc chloride in isopropyl alcohol, but can also be made by boiling propyl or isopropyl iodide with alcoholic potash.



The lower compound, *methylene*,  $\text{CH}_2$ , which might be expected, is unknown. When methylene iodide,  $\text{CH}_2\text{I}_2$ , is heated with metallic zinc or

copper, ethylene itself is formed, just as ethane is obtained on attempting to prepare free methyl.

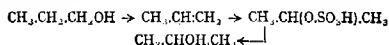


Similarly ethylene itself is produced by the action of sodium on ethylidene chloride, instead of the isomeric *ethylidene*,  $\text{CH}_3\cdot\text{CH}=\cdot$ , which might be expected. The failure of all attempts to prepare such compounds with free valencies is strong evidence for the doubly-linked formula of ethylene.

*Propylene*,  $\text{CH}_3\cdot\text{CH}:\text{CH}_2$  (Reynolds, 1851), is a gas which resembles ethylene, and condenses to a colourless liquid at  $-50^\circ$ . It combines with bromine in the same way (§ 104); *propylene bromide*,  $\text{CH}_3\cdot\text{CHBr}\cdot\text{CH}_2\text{Br}$ , is a liquid which boils at  $141^\circ$ , and resembles ethylene bromide.

Propylene also combines with sulphuric and hydrochloric acids, but instead of primary propyl compounds, secondary compounds are formed. Propyl alcohol may in this way be converted into secondary propyl alcohol.

In the same manner, and probably from the same cause, propylamine and its higher homologues yield mainly secondary alcohols when hydrolysed with nitrous acid.



Isobutyl alcohol can be converted into tertiary butyl alcohol in a similar manner, and the same action occurs with the higher homologues of ethylene, primary compounds being thus converted into secondary, and secondary into tertiary compounds.

When hydrogen chloride gas is passed into boiling amyl alcohol in presence of zinc chloride, a quantity of secondary amyl chloride is formed along with the primary chloride, from the intermediate formation of amylene; the function of the zinc chloride in the preparation of ethyl chloride (§ 23), would thus seem to be, in part at all events, to induce the formation of ethylene.

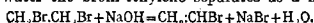
Owing to the recurrence of position isomerism, the isomerism of the higher homologues of ethylene is more complicated than that of the paraffins. There are three butylenes, and a mixture of these easily condensable gases can be isolated from the liquid which condenses on compressing oil-gas (Faraday, 1825).

*Ethyl-ethylene*,  $\text{CH}_3\cdot\text{CH}_2\cdot\text{CH}:\text{CH}_2$ , from normal butyl alcohol, boils at  $-5^\circ$ . *Symmetrical dimethyl-ethylene*,  $\text{CH}_3\cdot\text{CH}:\text{CH}\cdot\text{CH}_3$ , from secondary butyl alcohol, boils at  $1^\circ$ . *Isobutylene* or *unsymmetrical dimethyl-ethylene*,  $\text{CH}_3 > \text{C}:\text{CH}_2$ , from isobutyl and tertiary butyl alcohols, boils at  $-6^\circ$ . The butylenes readily form dibromides, and are converted by sulphuric acid, etc., into secondary and tertiary butyl compounds.

Apart from their unsaturated character and consequent chemical activity, the higher homologues of ethylene are physically like the paraffins, either light liquids or wax-like solids, according to their molecular weight. They occur in small amount in petroleum and coal-tar oil (§ 243), and are separated from the paraffins and other hydrocarbons by shaking with fuming sulphuric acid; with which, like ethylene, they combine, forming alkyl hydrogen sulphates.

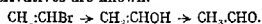
The ethylene hydrocarbons are known as *olefines*, i.e. homologues of olefiant gas (Guthrie, 1860); they are necessarily polymeric with the unknown methylene, and can consequently be represented by the general formula  $C_nH_{2n}$ .

**107. Substitution Products of the Olefines.**—Besides additive compounds, which are saturated paraffin derivatives, the olefines form a variety of substitution products, although rarely by direct action. When ethylene bromide is boiled with a solution of caustic soda in moderately strong alcohol it loses an equivalent of hydrogen bromide per molecule, and is converted into an unsaturated compound, monobrom-ethylene. The vapour is passed into ice-cold alcohol, and on pouring the solution into a large volume of ice-water the brom-ethylene separates as a heavy liquid.

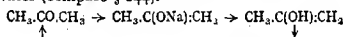


*Brom-ethylene* or *vinyl bromide*,  $CH_2:CHBr$  (Regnault, 1834), is a volatile liquid, which resembles ethyl bromide, but boils at  $23^\circ$ . It is distinguished sharply from the paraffin derivative in rapidly decolorising bromine, with which it forms an additive compound; *bromethylene dibromide* is a liquid which boils at  $188^\circ$ , and resembles ethylene bromide.

The hydroxy-compound corresponding with vinyl bromide is unknown in the pure state, and cannot be prepared by the usual reactions. When the bromide is heated with lead oxide and water, an agent which usually effects the replacement of halogen by hydroxyl, the isomeric acetaldehyde is formed, doubtless by molecular rearrangement of the transiently formed hydroxide. *Vinyl alcohol*,  $CH_2:CHOH$ , is present, however, in crude ether, and some of its derivatives are known.



The crystalline compound,  $C_3H_5NaO$ , which is obtained by the action of sodium on acetone (preferably dissolved in dry ether) is probably *sodium methylvinyl oxide*,  $CH_3.C(ONa):CH_2$ ; it is at once reconverted into acetone by water (compare § 144).



There are necessarily no derivatives of ethylene itself corresponding with aldehyde and acetic acid, but its higher homologues, containing alkyl radicals, give rise to series of unsaturated alcohols, acids, etc., such as allyl alcohol,  $CH_2:CH.CH_2OH$  (§ 131 *et seq.*). Mesityl oxide, the first condensation product of acetone (§ 89), is *isopropylidene-acetone* (*methyl-pentenone*, §§ 101, 111),  $CH_3.CO.CH:CH.CMe_2$ ; phorone, the second condensation product, is the corresponding *di-isopropylidene-acetone* (*dimethyl-heptadienone*),  $CMe_2:CH.CO.CH:CMe_2$ .

**108. Synopses.**—The olefinic hydrocarbons are formed by decomposition of alkyl hydrogen salts, and by the action of alkalis on the alkyl halides. They are distinguished from paraffins by forming additive compounds with bromine, and decolorising alkaline permanganate; and on this account are termed unsaturated hydrocarbons. The unsaturated condition is symbolised by a double linkage connecting adjacent carbon atoms.



## CHAPTER XX

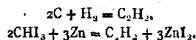
### THE ACETYLENES

**109. Acetylene.**—The hydrocarbon acetylene was originally obtained by the action of water on potassium carbonyl (§ 305), the black, explosive bye-product in the manufacture of potassium. It was afterwards observed to be formed from gaseous hydrocarbons by sparking, or imperfect combustion (Berthelot, 1867), and is produced in this way when a Bunsen flame is allowed to burn in its air-tube, or air is burned in an atmosphere of coal-gas.

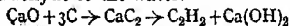
Acetylene is generated in larger quantities by the prolonged action of alcoholic potash on ethylene bromide, as the vinyl bromide, which is initially formed, loses a second equivalent of hydrogen bromide; the debromination is more quickly effected by passing the vapour of the dibromide over red-hot soda-lime, as in making ethylene from ethyl bromide.



Acetylene is also produced when iodoform is heated with a mixture of reduced copper and zinc dust; and it is formed by direct synthesis from its elements when an electric arc is maintained between carbon terminals in an atmosphere of hydrogen (Berthelot, 1868). The yield, however, is very small in both cases; and the product of direct synthesis is largely methane.

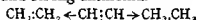


The best way of making the hydrocarbon is by synthesis from carbon and water. When coke is fused with lime in an electric furnace, *calcium carbide* or *acetylide*,  $\text{CaC}_2$ , a grey semi-crystalline solid, is formed (Moissan, 1894), which is hydrolysed by water, at the ordinary temperature, and with great energy, to acetylene and slaked lime; the water is simply allowed to drop slowly on lumps of the carbide in a suitable generating vessel; the action may be moderated by adding formaldehyde to the water.



*Acetylene* or *ethine*,  $\text{CH}:\text{CH}$  (E. Davy, 1839), is a colourless, insoluble gas, of sour, oppressive odour, which, when strongly cooled, condenses to a liquid boiling at  $-84^\circ$ ; it is fairly soluble in alcohol, and extremely so in acetone.

Acetylene bears the same relation to ethylene as the latter to ethane, and can be converted into either gas by direct addition of hydrogen; ethane is formed when a mixture of acetylene and hydrogen is left in contact with platinum black, and ethylene when copper acetylide (§ 110) is warmed with zinc dust and strong ammonia.



Acetylene is extensively used as an illuminating agent; it burns with an intensely luminous flame when led through a suitable jet, although when it is burned from an open vessel the flame is very smoky. As acetylene is convertible into ethylene, and ethylene into ethyl hydrogen sulphate and alcohol, it affords a means of preparing alcohol synthetically.

**110. Derivatives of Acetylene: its Constitution.**—From its relation to ethylene, acetylene is represented by the formula



Structural Formula of Acetylene.

the two carbon atoms being connected by three valencies—a triple linkage.

The symbolic nature of these linkages must be borne in mind, for the stability of a linkage does not increase with the number of valencies. The reverse is the case. Ethylene is much more readily attacked by agents than ethane, and acetylene is endothermic, and so unstable that it is decomposed explosively into its elements when a detonator is fired in it. Liquid acetylene appears to be a dangerous explosive. The same is true of the various derivatives, those of ethane being stable, whilst many of the acetylene compounds are explosive. The whole subject of the stability of linkages is reviewed later (§ 288).



Acetylene has feeble acid properties, and forms compounds with most of the metals. When sodium is gently heated in the gas, *sodium acetylide*,  $\text{CH}:\text{CNa}$ , is formed, a white solid from which the hydrocarbon is explosively regenerated by water.

On passing acetylene into a solution of ammonio-silver nitrate, a yellow precipitate of *silver acetylide*,  $\text{C}_2\text{Ag}_2$ , is thrown down; in the same way ammonio-cuprous chloride yields reddish-brown *cuprous acetylide*,  $\text{C}_2\text{Cu}_2$ . These compounds are highly explosive when dry, and detonate if heated or struck.

Copper acetylide forms a sensitive test for acetylene. If a beaker wetted with a solution of cuprous chloride in ammonium

chloride is inverted over a Bunsen burner in which the flame is burning below, the presence of acetylene, evident from the odour, is confirmed by the precipitation of the red acetylide.

This acetylide also affords a convenient means of separating the hydrocarbon from other gases, as it is quantitatively decomposed into acetylene and cuprous chloride when warmed with concentrated hydrochloric acid; the precipitate must not have become dry. In the absence of calcium carbide, copper acetylide, and thus pure acetylene, may be made in considerable quantity, by aspirating the products of combustion of air in coal gas through the cuprous solution.

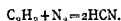
Although acetylene is more unsaturated than ethylene, it forms additive compounds much less readily, and may be shaken with bromine water for some time without decolorising it. When passed into cold bromine, however, it is converted into *acetylene tetrabromide* or *tetrabrom-ethane*,  $\text{CHBr}_2\cdot\text{CHBr}_2$ , a liquid which resembles ethylene bromide, but boils at  $137^\circ$ ; whilst by adding the halogen to an alcoholic solution of the hydrocarbon, the intermediate *dibromethylene*,  $\text{CHBr}:\text{CHBr}$ , is formed, a liquid resembling vinyl bromide. Acetylene also takes up a molecule of hydrogen bromide when heated with the concentrated acid at  $100^\circ$ , and is converted into vinyl bromide.

Like ethylene, the hydrocarbon is absorbed by fuming sulphuric acid, and when the resulting solution is diluted and distilled with water, acetaldehyde is obtained, together with some crotonaldehyde (§ 133) formed by its dehydration.



Similarly when the gas is passed into chromic acid mixture, it is oxidised to acetic acid, whilst with alkaline permanganate, the alkali oxalate is formed.

Acetylene combines with nitrogen when an electric arc is maintained in an atmosphere of the mixed gases, forming hydrogen cyanide by direct addition (Qewar, 1880).



It readily polymerises when passed through a red-hot combustion tube, forming benzene,  $\text{C}_6\text{H}_6$ , and other compounds.

**111. Homologues of Acetylene.**—Several homologues of acetylene of the general formula  $\text{C}_n\text{H}_{2n-2}$  are known.

*Alkylenes* or *propyne*,  $\text{CH}_3\cdot\text{C}:\text{CH}$  (Markownikoff, 1861), is an easily condensable gas, which is formed by heating propylene bromide with alcoholic potash, whence its constitution. It is very soluble in concentrated sulphuric acid, and the solution when diluted and distilled yields acetone and mesitylene (§ 328). Alkylenes resemble acetylene in every essential, forms metallic compounds, and is oxidised to propionic acid by chromic acid.

There is, however, a second hydrocarbon of the formula  $\text{C}_3\text{H}_4$ . *Allylene* or *isoallylene*,  $\text{CH}_2\cdot\text{C}:\text{CH}_2$  is a gas, which, like allylene, is hydrolysed by sulphuric acid and water to acetone; but it does not form metallic compounds, whilst on the other hand it forms additive compounds with much



greater readiness. *Allene tetrabromide*,  $\text{CH}_2\text{Br}.\text{CBr}_2.\text{CH}_2\text{Br}$ , is a liquid resembling ethylene bromide, and boiling at  $220^\circ$ . Allene is therefore a *diolefine*, and not a true homologue of acetylene. The suffix *-ene* denotes the presence of one or more ethylene linkages, in distinction to the suffixes *-ine* and *-ane*, which respectively indicate acetylene and paraffin linkages.

In the four-carbon and higher acetylenes and diolefines, position isomerism is possible, as in the higher olefines, and the formation of metallic derivatives is dependent on the presence of the mobile hydrogen of the  $\text{CH}$  or methine group. Thus *ethyl-acetylene* or *1-butine*,  $\text{CH}_3\text{C}.\text{CH}_2.\text{CH}_3$ , a liquid boiling at  $18^\circ$ , forms such derivatives, whilst *dimethylacetylene* or *2-butine*,  $\text{CH}_3.\text{C}.\text{C}.\text{CH}_3$ , does not do so.

As in all the homologous series, the higher acetylenes are oily liquids or wax-like solids. Like propylene and the higher olefines, they give rise to a series of alcohols, acids, etc., such as propargyl alcohol (§ 134).

**112. Synopsis.**—Acetylene, a doubly unsaturated hydrocarbon having a triple linkage in its formula, is formed by removing hydrogen bromide from ethylene bromide. Acetylene and certain of its homologues are distinguished from olefines and paraffins by forming explosive compounds with metals.



## PART II

### Complex Aliphatic Compounds

#### SECTION VI

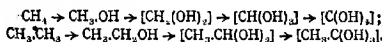
#### COMPLEX SUBSTITUTION PRODUCTS OF ETHANE

#### CHAPTER XXI

##### HALOGEN SUBSTITUTION PRODUCTS

**113. Simple and Complex Compounds.**—The properties of the simple compounds thus far considered are defined by the nature of their characteristic radicals, and are comparatively little influenced by that of the residual part of the molecule. Once the radical is known, the chemical behaviour of the compound can be deduced with remarkable accuracy. Any primary alcohol gives the same set of derivatives as ethyl alcohol, a fact which may be summarised in the statement that primary alcohols have the general formula  $R\cdot CH_2OH$ . Similarly acids have the general formula  $R\cdot COOH$ , and aldehydes and ketones the general formula  $R\cdot CHO$  and  $R\cdot CO\cdot R$  respectively.

We have also seen that these compounds may be regarded as substitution-products of the hydrocarbons. Methyl alcohol and its immediate derivatives are substituted methanes, and the compounds of the ethyl and higher groups are similarly derived from the homologous hydrocarbons. As far as methane is concerned it is immaterial which view is adopted, but when there is more than one carbon atom in the molecule the substitution method indicates further possibilities; for regarding acetic acid as a substituted ethane, the substitution is seen to have taken place in only one of the methyl radicals.

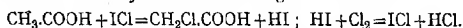


Methyl alcohol, formaldehyde, formic acid and carbon dioxide comprise the whole of the oxygenated derivatives of methane which are theoretically possible, whereas only a moiety of the ethane hydrogen has been replaced when acetic acid is reached. There is no apparent reason why the substitution should be thus limited, whilst at the same time it is obvious that if it be continued in the other half of the molecule, the products can no longer be simple in character. Such complex substitution products form the subject of the following chapters.

**114. The Halogen-Acetic Acids.**—When a mixture of acetic acid vapour and chlorine is exposed to direct sunlight, the colour of the chlorine slowly disappears, just as with ethane under similar conditions; hydrogen chloride is formed, and a substitution-product, trichloroacetic acid, is deposited in crystals on the sides of the flask. The chlorination is much more rapidly effected in presence of a carrier, such as iodine (Müller, 1862), red phosphorus (Volhard, 1885), or hydrogen chloride (Lapworth, 1903).

The action of the carrier varies. Iodine forms iodine chloride, which chlorinates the acid more vigorously than free chlorine, and is continuously regenerated by the chlorine from the hydrogen iodide into which it is converted. Phosphorus forms phosphorus trichloride, which converts some of the acid into acetyl chloride, a compound which is more easily chlorinated than the free acid; the chloroacetyl chloride interacts with the acid, forming chloroacetic acid and regenerating acetyl chloride. Hydrogen chloride, which is conveniently formed by adding acetyl chloride to ordinary glacial acetic acid (*i.e.* containing a little water), acts ionically.

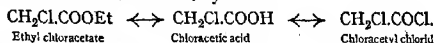
Either of the chlorinated acetic acids may be obtained, according to the amount of chlorine used, but the method is usually applied only to the preparation of monochloroacetic acid; the chlorination is carried on in a reflux apparatus until the necessary increase in weight is observed.



The product, which readily crystallises on being cooled in ice and stirred, is purified by fractionation, the tail fraction, distilling above  $180^\circ$ , being melted, crystallised, and drained, in the same way as acetamide (§ 53), until the melting point is constant; the lower fractions are worked up again.

*Chloroacetic acid*,  $\text{CH}_2\text{ClCOOH}$  (R. Hoffmann, 1855), which is a deliquescent, very corrosive, crystalline solid, melts at  $63^\circ$ , and boils at  $187^\circ$ ; it is a much stronger acid than acetic acid,  $K=0.155$ , but resembles it in all essentials.

It forms metallic salts and esters, such as *potassium chloroacetate*, which is a crystalline solid, and *ethyl chloroacetate*, a stable liquid boiling at  $145^\circ$ ; and it is converted by phosphorus trichloride into *chloroacetyl chloride*, a fuming liquid which is reconverted into the acid by water.

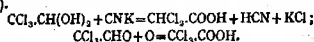


Chloroacetic acid thus still contains the acidic hydroxyl of the acetic acid molecule, and it is therefore a methyl hydrogen atom of the latter which is replaced by chlorine.

Dichloroacetic and trichloroacetic acids were first obtained by directly chlorinating acetic acid, but are more conveniently

prepared from chloral hydrate, the aldehydrol of trichloroacetic acid (§ 115).

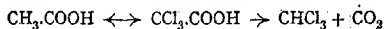
When chloral hydrate is boiled with potassium cyanide solution, dichloroacetic acid is formed, by a somewhat unusual process of reduction; whilst when it is heated with fuming nitric acid it is oxidised to trichloroacetic acid (Kolbe, 1845).



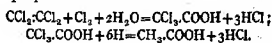
*Dichloroacetic acid*,  $\text{CHCl}_2\cdot\text{COOH}$  (Müller, 1862), is a heavy liquid which boils at  $191^\circ$  and freezes at  $-4^\circ$ ; its dissociation constant is  $K = 5 \cdot 14$ . *Trichloroacetic acid*,  $\text{CCl}_3\cdot\text{COOH}$  (Dumas, 1838), is a deliquescent, corrosive, crystalline substance, which melts at  $55^\circ$ , and boils at  $195^\circ$ ; it is a powerful acid, its dissociation constant being  $K = 121$ . Like the mono- and dichloroacids, it forms stable salts, esters, etc.

*Ethyl trichloroacetate*,  $\text{CCl}_3\cdot\text{COOEt}$ , is an insoluble oily liquid boiling at  $167^\circ$ , which is readily prepared by mixing equal weights of trichloroacetic acid, alcohol and sulphuric acid, warming until opalescent, and then pouring the product into cold water; when shaken with aqueous ammonia it is converted into *trichloroacetamide*,  $\text{CCl}_3\cdot\text{CONH}_2$ , a crystalline substance which melts at  $135^\circ$ , and sublimes with great readiness.

When trichloroacetic acid is boiled with alkalis it is hydrolysed to chloroform, the carboxyl group being eliminated as carbon dioxide (Dumas, 1838). The three hydrogen atoms which are replaced by chlorine are therefore again those of the methyl radical of acetic acid, a conclusion which is substantiated by the reduction of trichloroacetic acid to this acid when digested with sodium amalgam (Melsens, 1842).



Trichloroacetic acid can also be made from carbon tetrachloride, and thus synthetically from carbon disulphide and carbon. When the vapour of the tetrachloride is passed through a red-hot tube it is converted into *tetrachlorethylene*,  $\text{CCl}_2\cdot\text{CCl}_2$ , a liquid boiling at  $121^\circ$ ; and on passing chlorine into this liquid covered with water, in a flask which is exposed to direct sunlight, trichloroacetic acid is formed by successive chlorination and hydrolysis (Kolbe, 1845). Acetic acid was first synthesised by reducing trichloroacetic acid prepared in this manner.



The various bromoacetic and iodoacetic acids are crystalline substances resembling the chloroacetic acids. Monobromoacetic acid is prepared by heating glacial acetic acid and acetyl chloride on a water-bath with the theoretical amount of bromine (Fig. 16); it is purified by fractionation. The iodo-

compounds are usually prepared indirectly, as owing to the powerful reducing action of hydrogen iodide, direct substitution by iodine can only be effected, and then with difficulty, in presence of iodic acid or some similar agent which reconverts the hydrogen iodide into iodine.

*Bromacetic acid*,  $\text{CH}_2\text{Br.COOH}$ , is a very deliquescent, corro-

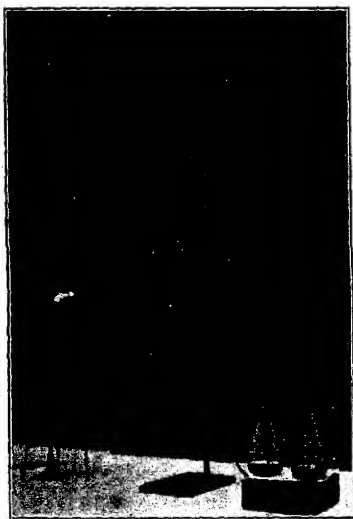


Fig. 18.—Bromination of Acetic Acid.

The hydrogen bromide and bromine fumes are absorbed by the water in the Volhard trap, which is so arranged that whilst all gases escaping from the apparatus are washed by the liquid, the latter cannot possibly be drawn into the reflux apparatus.

sive substance melting at  $51^\circ$ ; its dissociation constant is  $K=0.138$ . *Iodacetic acid*,  $\text{CH}_2\text{I.COOH}$ , melts at  $82^\circ$ ; its dissociation constant is  $K=0.075$ .

**115. Chloral and Choral Hydrate.**—Trichloraldehyde or chloral, the aldehyde of trichloroacetic acid, is formed when aldehyde is chlorinated in presence of marble; the marble serves to take up the hydrochloric acid, which otherwise brings about conden-

sation (§ 146). Chloral is usually manufactured, however, by chlorinating alcohol. Dry chlorine is passed into anhydrous alcohol in a reflux apparatus, the spirit at first being kept cool, but afterwards heated at  $60^{\circ}$ , and finally, as the action moderates, at  $100^{\circ}$ ; the *chloral alcoholate* thus formed is then hydrolysed by concentrated sulphuric acid.

The chlorination is continued until ethyl chloride ceases to be evolved—an operation requiring many hours; the product is then heated with concentrated sulphuric acid for several hours at the same temperature, and the oily layer of chloral which separates is removed, and redistilled from calcium carbonate.

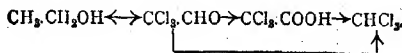
The chloral is finally converted into the crystalline hydrate by mixing with an equimolecular proportion of water; much heat is evolved, and the product soon becomes solid. It combines with alcohol in the same manner.

*Chloral* or *trichloroacetaldehyde*,  $\text{CCl}_3\text{CHO}$  (Liebig, 1831), is a pungent, heavy, oily liquid, boiling at  $97^{\circ}$ ; its *hydrate* or *aldehyde*,  $\text{CCl}_3\text{CH}(\text{OH})_2$ , is a crystalline substance melting at  $57^{\circ}$ . Chloral hydrate has a peculiar sweetish odour, resembling that of stale apples, and an acrid, unpleasant taste; it is used as a hypnotic (Liebreich, 1869).

Chloral shows the usual properties of aldehydes; it reduces ammoniacal silver nitrate, colours bleached rosaniline, forms *additive compounds* with ammonia, hydrogen cyanide, and sodium bisulphite, and an *oxime* with hydroxylamine.

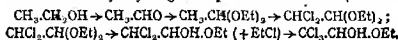
Chloral hydrate is one of the few examples of hydroxy-compounds in which two hydroxyl groups are linked to the same carbon atom, and completely justifies the view that the aldehydes represent dihydroxy-derivatives of the hydrocarbons. When vaporised, the hydrate is dissociated into chloral and steam, for its boiling point is about the same as that of water or chloral, and its vapour density the mean, instead of the sum, of the vapour densities of its constituents. But it is converted into a *diacetate*,  $\text{CCl}_3\text{CH}(\text{OAc})_2$ , by acetyl chloride, and is thus a stable chemical compound when solid. Chloral forms a similar crystalline *alcoholate*,  $\text{CCl}_3\text{CH}(\text{OH})\text{OEt}$ , closely resembling the hydrate.

Although oxidisable to trichloroacetic acid in the normal manner, chloral is converted into ordinary alcohol when reduced with sodium amalgam, the chlorine appearing to be replaced before the aldehyde group is affected; and as already noted, it is hydrolysed to chloroform and the alkali formate when mixed with cold caustic alkali.



The formation of chloral from alcohol is somewhat complex, but may be summarised by saying that the alcohol is first oxidised to aldehyde, and then chlorinated. Several stages intervene, however, between the aldehyde and the final product of this vigorous action.

The aldehyde combines at once with some of the unchanged alcohol, forming acetal, and the latter is successively chlorinated to *mono-* and *dichloroacetal*. The dichloroacetal is resolved by the liberated hydrogen chloride, as the temperature rises, into ethyl chloride and *dichloroacetaldehyde alcoholate*,  $\text{CHCl}_2\cdot\text{CHOH}\cdot\text{OEt}$ , which is then converted by further chlorination at the highest temperature into the corresponding trichloro-compound, chloral alcoholate. Finally the alcoholate is resolved by the sulphuric acid into ethyl hydrogen sulphate and chloral (Fritsch, 1894).



The formation of chloroform from alcohol and bleaching powder is probably parallel, the chloral first formed being hydrolysed by the lime. The formation of iodoform is also probably analogous, although the iodol corresponding with the chloral is unknown; it is quite possible, however, that it is transiently formed in the action.

118. Influence of Halogen-Substitution on the Properties of Compounds.—It was at one time thought that the substitution of hydrogen by a powerfully electronegative element like chlorine must fundamentally alter the character of the compound in which the substitution is effected. The preparation of trichloroacetic acid conclusively disproved this view, and thus led to the development of the theory of substitution (Dumas, 1838), without which the progress of Organic Chemistry would have been very slow. The results described in the preceding paragraphs show that the unsubstituted part of the paraffin molecule in the acids and their relatives is attacked by chlorine in precisely the same way as the paraffin itself, yielding chloro-substitution products which are still aldehydes, acids, etc., in spite of the replacement of hydrogen by chlorine.

Although the substitution of chlorine for hydrogen makes little difference qualitatively to the properties of the substance, it has nevertheless a marked quantitative effect. In the first place it intensifies the acid character of the molecule, and renders it more reactive; and in the second place it decreases its stability. The increased activity and instability are mutually interdependent, and are probably due to the same cause; very inactive substances such as the paraffins are also particularly stable.

The increase in the acidity of the acids is particularly worthy of attention. We have already noticed that the substitution of an oxygen atom for two hydrogen atoms converts the primary alcohol radical,  $\text{CH}_2\text{OH}$ , into the acid or carboxyl radical,  $\text{COOH}$ , and the feebly basic substance alcohol into the well-defined acid, acetic acid. The substitution of chlorine for the hydrogen of the acetic acid molecule is merely an extension of this process, and the substance continues to grow more acid as the radical



becomes more strongly electronegative in character. The acidifying influence of bromine is not so great as that of chlorine, as might be expected, and the acidifying influence of iodine is smaller still.

A rough idea of the relative strength of acids is gained by the action of their decinormal (or, if necessary, normal) solutions on Congo-red paper, which is made by dipping strips of filter paper in an alcoholic solution of Congo-red dye (§ 384), and drying. Very strong acids such as sulphuric, hydrochloric and trichloroacetic acids turn the red to an intense blue, but weaker acids produce less intense blues and greys.

Acid	Dissociation Constant, K
Acetic	0.0018
Chloroacetic	0.155
Dichloroacetic	5.14
Trichloroacetic	121
Bromoacetic	0.138
Iodoacetic	0.075
Butyric	0.0015
Trichlorobutyric	10

The instability of the chloro-compounds increases step by step with their acidity, and when all the hydrogen of the methyl radical has been substituted, the stable union of carbon atoms characteristic of the paraffins has disappeared. Trichloroacetic acid and its aldehyde chloral are at once decomposed by caustic alkalis, or even by water at a high temperature. Mono- and dichloroacetic acids are not broken up by hydrolytic agents, but like the ethyl chloride and ethylidene chloride from which they are derived are converted by those agents into substances of alcoholic and aldehydic character (Chapter XXII).

**117. Homologues and Analogues of Chloral.**—The condensation product, which is formed when aldehyde is chlorinated alone, is a homologue of chloral, and is known as butyl chloral.

The chlorine is passed into cold paraldehyde, and after the action has moderated, the liquid is heated at 100°, and the chlorination continued until action ceases; the product is poured into alcohol and neutralised with calcium carbonate, and the alcoholate which is thus formed is fractionated, and decomposed with concentrated hydrochloric acid.

The action is again complex. Probably chloraldehyde is first formed, which under the influence of the liberated hydrochloric acid unites with a second molecule of aldehyde, forming a condensation product, *chloroacetaldehyde*,  $\text{CH}_3\text{CH}:\text{CCLCHO}$  (see §§ 132, 146); this chlorinated aldehyde combines with a molecule of chlorine, forming trichlorobutaldehyde or butyl chloral (Finner, 1875).



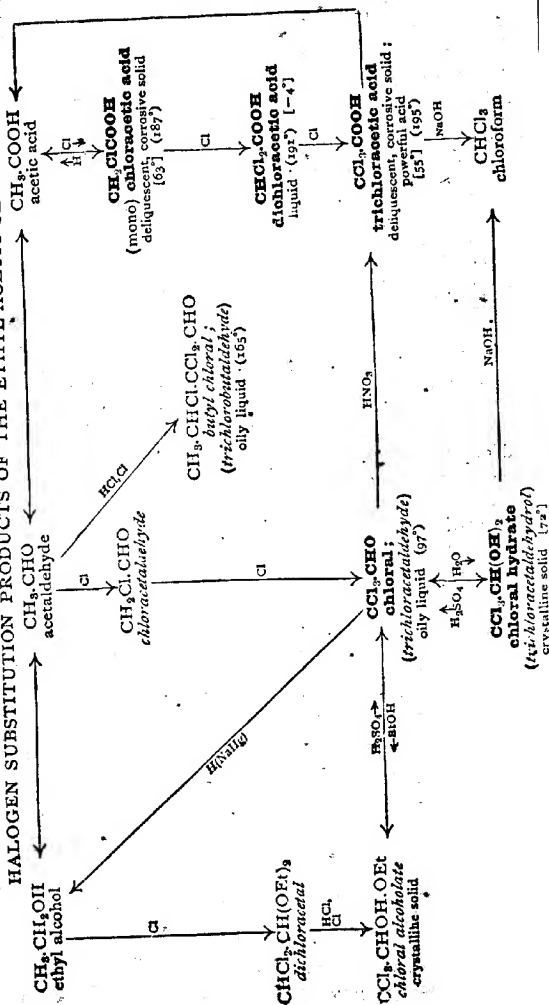
*Butyl chloral*,  $\text{CH}_3\text{CHCl.CCl}_2\text{CHO}$  (Pinner, 1870), is a liquid which closely resembles ordinary chloral, but boils at  $165^\circ$ . Its *hydrate*,  $\text{CH}_3\text{CHCl.CCl}_2\text{CH(OH)}_2$ , is a colourless crystalline solid, which melts at  $78^\circ$ , and resembles camomile in odour; like chloral hydrate, it is used as a hypnotic.

Butyl chloral reduces silver, and colours bleached rosaniline, but it is hydrolysed by alkalis to the alkali formate and *dichloropropylene*,  $\text{CH}_2\text{CCl.CHCl}$ , a liquid of aromatic odour; the trichloropropane which might be expected loses hydrogen chloride. Butyl chloral is oxidised by fuming nitric acid to *trichlorobutyric acid*,  $\text{CH}_3\text{CHCl.CCl}_2\text{COOH}$ , a very acid, crystalline substance resembling trichloroacetic acid; and it is reduced by sodium amalgam to normal butyl alcohol.

When a solution of cetyl alcohol in chloroform is chlorinated under the same conditions as ordinary alcohol, a chlorinated derivative of palmitic aldehyde is formed; it is not homologous with the lower chlorals, as it contains relatively more chlorine. *Palmitic chloral*,  $\text{C}_{15}\text{H}_{31}\text{Cl}_{12}\text{CHO}$  (Claus, 1891) is a thick yellow oil, which like the lower chlorals forms a crystalline *hydrate* with water.

**118. Synopsi.**—By continued chlorination of the alcohols, aldehydes and acids, chlorinated aldehydes and acids, such as chloral and the chloroacetic acids are produced; owing to the influence of the electronegative halogen, the acids are less stable and more reactive than the original unsubstituted acids. Many of the corresponding bromine and iodine derivatives are also known.

HALOGEN SUBSTITUTION PRODUCTS OF THE ETHYL-ACETIC SERIES.



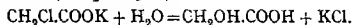
## CHAPTER XXII

### HYDROXY-SUBSTITUTION PRODUCTS : THE GLYCOL-OXALIC SERIES

**119. Glycollic Acid.**—Alcohol, aldehyde and acetic acid being derived from ethane by oxidation of one of its methyl groups, compounds may be expected in which the second methyl group is also oxidised; such compounds must bear the same relation to the chloracetic acids and their derivatives, as alcohol to chlorethane, etc., and should act in a dual manner.

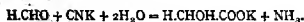
Glycollic acid, the hydroxy-acid corresponding with chloracetic acid, is a primary alcohol, as well as an acid, and has derivatives in each of these capacities; whilst in the remaining members of the series, the alcohol, aldehyde and acid groups are combined with each other in every conceivable way.

Glycollic acid is prepared by boiling a concentrated solution of potassium chloracetate or bromacetate in a reflux apparatus for many hours (compare § 22).



The product, which contains potassium chloride or bromide and the free acid, is evaporated to dryness under reduced pressure, and the glycollic acid is extracted from the residue with acetone, in which the halogen salt is insoluble.

The acid was first obtained from glycocholl (§ 217). It occurs naturally in unripe fruit, and may be made by gently oxidising alcohol with nitric acid, or by oxidising glycerol or invert-sugar with silver oxide in presence of calcium carbonate. It is also formed synthetically when aqueous formaldehyde is warmed with potassium cyanide (compare Lactic Acid, § 137).



*Glycollic* or *hydroxyacetic acid*,  $\text{CH}_2\text{OH.COOH}$  (Strecker, 1851), is a deliquescent, crystalline substance, which melts at about  $80^\circ$ , and has a dissociation constant  $K=0.0152$ ; owing to the acidifying influence of the additional oxygen atom it is therefore a decidedly stronger acid than acetic acid.

The molecular formula of glycollic acid is  $\text{C}_2\text{H}_4\text{O}_3$ . As it behaves as a monobasic acid, forming metallic salts, such as

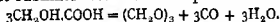
*potassium glycollate*,  $C_2H_3KO_3$ , and esters such as *ethyl glycollate*,  $C_2H_3EtO_3$ , it contains the carboxyl radical, and is represented by a rational formula,  $CH_3O.COOH$ .

Ethyl glycollate interacts vigorously with acetyl chloride, with evolution of hydrogen chloride, forming an *acetyl derivative*, in which a hydrogen atom of the ethyl glycollate molecule is replaced by acetyl; as this interaction is characteristic of alcohols (§ 41), the third oxygen atom of the ethyl glycollate molecule is present as alkylic hydroxyl.

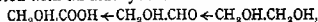
The constitutional formula of the ester is therefore  $CH_2OH.COOEt$ , and that of its acetyl compound,  $CH_2(OAc).COOEt$ .

The presence of both alkylic and acidic hydroxyl groups is confirmed by the action of phosphorus pentachloride on the acid. In the cold, this agent yields *glycollic chloride*,  $CH_2OH.COCl$ , a fuming liquid which is reconverted into the acid by simple digestion with water, and is therefore an acid chloride; but on heating the phosphorus chloride with the acid, *chloracetyl chloride*,  $CH_2Cl.COCl$ , is formed, identical with that which is formed directly from chloracetic acid (§ 114).

Glycollic acid can not only be made from formaldehyde, but can also be converted into it, for when it is heated with concentrated sulphuric acid at  $150^\circ$ , a brisk effervescence sets in, and carbon monoxide escapes, whilst paraformaldehyde sublimes into the cooler parts of the vessel.



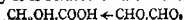
From its dual character as an acid and a primary alcohol the oxidation and reduction products of glycollic acid are numerous. Not only as an acid is it connected with an aldehyde and alcohol—



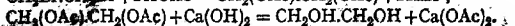
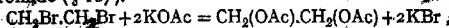
but as a primary alcohol it is oxidisable to a second aldehyde and acid—



whilst in its dual capacity it is related to a third or double aldehyde—



**120. Glycerol.**—The double or diprimary alcohol corresponding with glycollic acid is made by hydrolysing ethylene bromide, either directly, by prolonged boiling with aqueous potassium carbonate, or indirectly, by boiling the dibromide with sodium acetate and acetic acid, and hydrolysing the resulting *glycol diacetate* with baryta or dry slaked lime (Erlenmeyer, 1878). The acetate method is the best, as in the direct process much of the ethylene bromide is converted into vinyl bromide (§ 107).



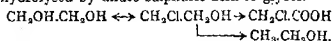
*Glycerol* or *ethylene alcohol*,  $CH_2OH.CH_2OH$  (Wurtz, 1856), is a sweet, syrupy, hygroscopic liquid, which boils at  $195^\circ$ , and

freezes at a low temperature to a crystalline solid, melting at  $11^{\circ}$ ; it is volatile with steam.

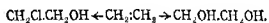
The presence of two alkylic hydroxyl groups is proved by the formation of two acetyl derivatives when glycol is boiled with acetic acid; the primary character of the alcohol groups is demonstrated by its oxidation by nitric acid to the corresponding aldehyde and acid, glyoxylic and oxalic acids. The name glycol registers the double analogy to glycerine (§ 127) and alcohol.

The dichloro-derivative of glycol, formed by the action of phosphorus pentachloride, is identical with ethylene dichloride, whilst the monochloro-compound, glycol chlorhydrin, may be regarded as chlorethyl alcohol; it is best formed by the action of sulphur dichloride on glycol (compare Glycerol, § 128).

*Glycol chlorhydrin* or *chlorethyl alcohol*,  $\text{CH}_2\text{ClCH}_2\text{OH}$  (Wurtz, 1859), is a sweet liquid, boiling at  $128^{\circ}$ . It is reduced by sodium amalgam to ethyl alcohol, and oxidised by chromic acid mixture to chloracetic acid, whilst it is hydrolysed by dilute sulphuric acid to glycol.



Both glycol and its chlorhydrin may be made directly from ethylene, and on this account are termed *ethylene glycol* and *chlorhydrin*. When ethylene is shaken with aqueous hypochlorous acid, it is converted into the chlorhydrin, whilst with dilute alkaline permanganate (§ 104) glycol is formed.



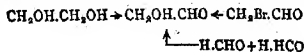
Ethylene chlorhydrin can be deprived of its halogen in the same way as the dibromide, but the product thus formed is of a different type to vinyl bromide; it is isomeric with acetaldehyde. *Ethylene oxide*,  $\text{C}_2\text{H}_4\text{O}$ , is a mobile liquid which boils at  $14^{\circ}$ , and like acetaldehyde is reduced to alcohol by sodium amalgam. It is readily reconverted into the chlorhydrin by hydrochloric acid, which it neutralises very rapidly, although not strictly speaking a base; it must be regarded as an internal ether of glycol.



**121. The Aldehydes of Glycol.**—As glycol is a diprimary alcohol, it forms three aldehydic derivatives, namely, an alcohol-aldehyde, an aldehyde-acid, and a double aldehyde.

The alcohol-aldehyde is formed by oxidising glycol with hydrogen peroxide in presence of ferrous sulphate (§ 129), or hydrolysing bromacetaldehyde with baryta water.

It is also produced by polymerisation of formaldehyde (compare Aldol, § 146), but is most conveniently prepared from dihydroxymaleic acid (§ 160).



*Glycollic aldehyde*,  $\text{CH}_2\text{OH}\cdot\text{CHO}$ , is a sweet, unstable crystalline substance, which has the typical properties of an aldehyde; it reduces ammoniacal silver solutions in the cold, and alkaline copper solutions on warming; and it immediately colours bleached rosaniline.

Glycollic aldehyde is of great theoretical interest as the first member of the sugar series (§ 188), of which grape-sugar is the most important; it is probably formed from tartaric acid during the ripening of grapes, and rapidly polymerises when warmed, into more complex sugars, such as are present in ripe fruit. Like grape-sugar it is converted into a yellow crystalline *osazone* (§ 185), when warmed with phenylhydrazine acetate.

Glyoxylic acid and glyoxal, the aldehyde-acid and double aldehyde corresponding with glycol, were originally prepared by oxidising alcohol with nitric acid (compare *Glyceric Acid*, § 129). The acid is more conveniently obtained by indirect hydrolysis of dichloroacetic acid, to which it bears the same relation as aldehyde hydrate to ethylidene chloride.

Potassium dichloroacetate is boiled with a concentrated solution of potassium acetate, and the *diacetate* of glyoxylic acid which is thus formed is hydrolysed by boiling water to potassium glyoxylate and free acetic acid, which may be removed by distillation.

Glyoxylic acid is also formed by the spontaneous oxidation of acetic acid by air in sunlight, and is therefore present in appreciable quantity in the first fractions obtained on rectifying commercial acetic acid (Hopkins, 1901). It may be prepared by reducing a saturated solution of oxalic acid with sodium amalgam; if a few drops of such a solution or some commercial acetic acid be mixed with a little albumen (white of egg) solution, an intensely violet ring is formed on addition of concentrated sulphuric acid (see Indole, § 407).

*Glyoxylic acid*,  $\text{CH}(\text{OH})_2\cdot\text{COOH}$  (Debus, 1856), is a syrup which crystallises only with difficulty; it is a stronger acid than glycollic acid,  $K = 0.0474$ , and forms the usual metallic salts; the ethereal salts are unknown.

As an aldehyde, it is oxidised by nitric acid to the corresponding acid, oxalic acid, and reduced by zinc dust and water to the corresponding primary alcohol, glycollic acid; it is reconverted into dichloroacetic acid by phosphorus pentachloride.



Glyoxylic acid gives the usual aldehyde reactions, and forms a crystalline *hydrazone* with phenylhydrazine; but with caustic soda, it resembles formaldehyde (§ 86), and is converted into glycollic and oxalic acids.

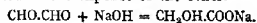


Glyoxal is conveniently made by oxidising aldehyde with

nitric acid at the ordinary temperature (Liubawin, 1878), and is separated from the neutralised product in the form of an insoluble bisulphite compound, by the formation of which it is distinguished from glycollic aldehyde.

*Glyoxal* or *glyoxylic aldehyde*,  $\text{CHO} \cdot \text{CHO}$  (Debus, 1856), is an amorphous solid, or when not quite free from water, a syrupy liquid; it gives the usual aldehyde reactions, such as the reduction of ammoniacal silver nitrate, and the colouring of bleached rosaniline.

Glyoxal is oxidised by nitric acid to glyoxylic or oxalic acid, according to the concentration. With alkalis or with water at  $150^\circ$  it resembles glyoxylic acid, and is converted into glycollic acid, one of the aldehyde groups being oxidised at the expense of the other.



**122. Oxalic Acid.**—The end product of the oxidation of all these substances, short of carbon dioxide, is oxalic acid, which also results from the oxidation of many other Organic compounds. Oxalic acid is thus slowly formed from acetic acid by the action of alkaline permanganate; concentrated sodium acetate solution is boiled down with caustic soda and potassium permanganate, until the green manganate has disappeared, and on adding acetic acid and calcium chloride to the filtered solution of the product, calcium oxalate is precipitated.

Oxalic acid occurs naturally in the common sorrel (*oxalis*), and in rhubarb and other plants; the commercial product is made from sawdust (cellulose, § 178) by oxidation with air and caustic alkali.

The sawdust is made into a paste with caustic potash and soda, and heated in open vessels at about  $240^\circ$ ; on extracting the product with cold water, the potash is dissolved out, and the sparingly soluble sodium oxalate left (Dale, 1856). The function of the potash is not quite clear, but it is indispensable to the action; probably the cellulose is hydrolytically oxidised to the alkali formate, which is readily convertible into the oxalate (§ 123). The sodium oxalate is boiled with milk of lime, by which it is converted into the insoluble calcium oxalate, the alkali being regenerated; and the calcium oxalate, after washing, is decomposed with dilute sulphuric acid, and the oxalic acid recrystallised.

In the laboratory, oxalic acid is conveniently made by oxidising sugar, starch, etc., with nitric acid (Scheele, 1776), a method which was formerly employed technically. When cane sugar is warmed with a considerable excess of somewhat diluted nitric acid, a violent action sets in, and dense nitrous fumes are evolved; and on concentrating the product and allowing it to cool, oxalic acid crystallises out



The success of the operation depends on stopping the concentration, and therefore the action, at the right point; if the oxidation is not carried far enough, a syrupy intermediate product, saccharic acid (§ 181), remains, whilst if it is carried too far, the oxalic acid is converted into carbon dioxide and lost. It is generally necessary in this and similar cases to start the crystallisation by adding a small crystal of the substance, or if this is not available, by rubbing the sides of the vessel with a glass rod to afford nuclei for the crystals.

*Oxalic acid*,  $\text{COOH}.\text{COOH} + 2\text{H}_2\text{O}$  (Scheele, 1776), crystallises from water in colourless, well-defined prisms, which lose their water of crystallisation at  $100^\circ$ . The anhydrous acid is slightly volatile, and sublimes slowly in slender needles when heated at  $100^\circ$ ; it is soluble in warm concentrated sulphuric acid (but is decomposed by the hot acid), and crystallises from this solvent in large prisms.

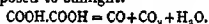
The molecular formula of oxalic acid follows from the composition of the two classes of metallic oxalates, and from the vapour densities of its ethereal salts. Its constitution as the simplest dicarboxylic acid is necessitated by considerations of valency, but is also established by its relation to glycol and glycollic acid; as previously stated, it is formed from these compounds by oxidation, and it is converted into the latter of them by reduction with zinc and dilute hydrochloric acid.



Oxalic acid is a strong acid, its dissociation constant,  $K=10$ , being nearly twice that of dichloroacetic acid; the influence of oxygen substitution is therefore of the same order as that of chlorine.

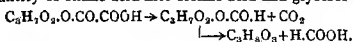
Acid	Dissociation Constant, K
Acetic	0.0018
Glycollic	0.0152
Glyoxylic	0.0474
Oxalic	10

*Oxalyl chloride*,  $\text{COCl}.\text{COCl}$ , a very unstable fuming liquid, boiling at  $70^\circ$ , is formed when ethyl oxalate is distilled with phosphorus pentachloride; on distilling the acid itself with either of the phosphorus chlorides, it is resolved into a mixture of hydrogen chloride and the oxides of carbon. An analogous result is obtained by heating it with concentrated sulphuric acid, affording the well-known method of preparing carbon monoxide; certain oxalates, such as the uranium salt, decompose spontaneously in this manner when exposed to sunlight.

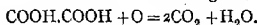


The similar decomposition into carbon dioxide and formic acid has been

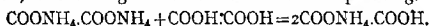
already noted; the acid probably forms an unstable ethereal salt with the glycerol, which immediately splits up into carbon dioxide and mono- and di-formin (§ 128), the formates of glycerol analogous to the glycol acetates. The formins are then either hydrolysed by the water of crystallisation of the acid to formic acid and glycerol, or decomposed by a further quantity of oxalic acid into formic acid and glycerol oxalate.



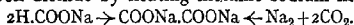
Oxalic acid, as the end product of the hydroxy-ethane series, cannot be further oxidised without breaking up the molecule, so that when warmed with acid permanganate it is resolved into carbon dioxide and water, the permanganate being decolorised. The action is slow at first, but very rapid as soon as some manganous sulphate has been formed; and as it is quantitative affords an accurate method of estimating the acid.



**123. The Oxalates.**—The alkali oxalates are made directly from the acid and caustic or carbonated alkali. *Ammonium oxalate*,  $\text{COONH}_4\cdot\text{COONH}_4$ , is prepared by simply neutralising a solution of the acid with ammonia, and evaporating to crystallisation; the acid salt, *ammonium hydrogen oxalate*,  $\text{COONH}_4\cdot\text{COOH}$ , is made by neutralising only half the solution, and adding the other half before evaporating.



*Sodium oxalate* also results, together with pure hydrogen, when sodium formate is heated, and it is directly synthesised from carbon dioxide by heating metallic sodium in that gas.



*Potassium hydrogen oxalate* is very sparingly soluble in water; it occurs in plants as *potassium quadrantoxalate* or salt of sorrel,  $\text{KHC}_2\text{O}_4\cdot\text{H}_2\text{C}_2\text{O}_4\cdot 2\text{H}_2\text{O}$ , in molecular combination with oxalic acid. *Ferrous oxalate* is bright yellow in colour, and almost insoluble in water, so that ferrous sulphate is a delicate test for soluble oxalates; in combination with potassium oxalate it forms a soluble yellow salt, *potassium ferrous oxalate*,  $\text{K}_2\text{Fe}(\text{C}_2\text{O}_4)_2\cdot 2\text{H}_2\text{O}$ , which on account of its energetic reducing properties is used as a developer in photography. *Potassium ferric oxalate*,  $\text{K}_3\text{Fe}(\text{C}_2\text{O}_4)_3\cdot 3\text{H}_2\text{O}$ , is an emerald green crystalline salt, which is rapidly reduced to the ferrous salt when exposed to light, and is hence used for reducing platinum chloride in platinotype printing. The colours of these salts are abnormal because the metal is combined with the oxalic acid in a complex ion. *Calcium oxalate* is insoluble, and hence serves for the detection and estimation both of the metal and the acid. *Silver oxalate* is very sparingly soluble, even in dilute nitric acid, and somewhat explosive.

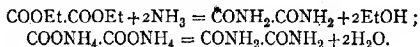
As oxalic acid is a strong acid, its esters can be prepared directly. Ethyl oxalate is readily made by heating the anhy-

drous acid with absolute alcohol in a distilling flask at  $100^{\circ}$ , while a stream of alcohol vapour is passed in from a second flask, to remove the liberated water. The temperature being gradually raised to  $130^{\circ}$ , the excess of alcohol and the water distil over, and when the distillation has ceased, the ethyl oxalate, which mostly remains in the flask, is fractionated.

*Ethyl oxalate*,  $\text{COOEt} \cdot \text{COOEt}$ , is a colourless liquid, which boils at  $186^{\circ}$ , and has a specific gravity of 1.079 at  $20^{\circ}$ ; when boiled with caustic soda solution in a reflux apparatus, it is hydrolysed in the usual manner to alcohol and sodium oxalate. *Methyl oxalate*, which is formed in the same way, is a colourless, crystalline solid, which melts at  $54^{\circ}$ ; it is often the case that methyl salts are solid when their homologues are liquid.

Some *ethyl hydrogen oxalate*,  $\text{COOEt} \cdot \text{COOH}$ , is formed in the preparation of the diethyl salt: it is a heavy, colourless liquid, which is decomposed when distilled under ordinary pressure, but can be distilled unchanged by diminishing the pressure (§ 143); under 15 mm. pressure it boils at  $117^{\circ}$ .

**124. Oxamide : Oxamic Acid : Cyanogen or Oxalonitrile.**—When ethyl oxalate is shaken with aqueous ammonia, oxamide is precipitated; the action is the same as with ethyl acetate, and alcohol can be separated from the filtrate by distilling it with excess of dilute sulphuric acid. The amide is also formed by heating normal ammonium oxalate, in the same way as acetamide from ammonium acetate.

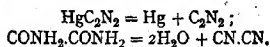


*Oxamide*,  $\text{CONH}_2 \cdot \text{CONH}_2$  (Bauhof, 1817), is an insoluble crystalline powder. Like all the amides it is hydrolysed by boiling alkali to ammonia and the alkali salt of the acid.

It is a diamide, however, and contains two amido-groups; when ammonium hydrogen oxalate is heated, an intermediate product, oxamic acid, is formed, which is both an amide and an acid.

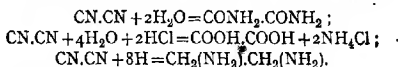
*Oxamic acid*,  $\text{CONH}_2 \cdot \text{COOH}$  (Balard, 1842), is a crystalline powder which melts and decomposes at  $220^{\circ}$ , and is hydrolysed by alkalis in the same way as oxamide; its ethyl salt, *ethyl oxamate*,  $\text{CONH}_2 \cdot \text{COOEt}$  (Boullay, 1828), a crystalline substance melting at  $115^{\circ}$ , is formed by passing ammonia gas into ethyl oxalate.

The oxalonitrile obtained by heating oxamide with phosphorus pentoxide is identical with cyanogen, and is best made by heating dry mercuric cyanide, or warming potassium cyanide with aqueous copper sulphate (§ 201).



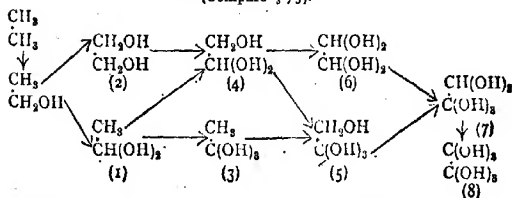
*Cyanogen* or *oxalonitrile*,  $\text{CN.CN}$  (Gay-Lussac, 1815), is an intensely poisonous gas, which condenses at  $-21^\circ$  to a colourless liquid freezing at  $-32^\circ$ ; it burns with a coloured (pink-mantled) flame, but in the absence of oxygen is stable even at very high temperatures, and occurs in blast-furnace gases.

Cyanogen is hydrolysed by alkalis to the alkali cyanide and cyanate (§ 207), and combines energetically with hot potassium and sodium, forming the alkali cyanide; in these respects it resembles the halogens. But otherwise it behaves as a typical nitrile; it is reconverted into crystalline oxamide when passed into cold concentrated hydrochloric acid, whilst oxalic acid itself is obtained if the product be boiled; when reduced with zinc and dilute hydrochloric acid it is converted into the corresponding amine, ethylene diamine (§ 215).



**125. Relation of the Glycol-Oxalic Series to Ethane.**—The members of the glycol-oxalic series are thus the hydroxyethanes, or their dehydration products, corresponding with the chlor-ethanes, and the more stable of them can be made by direct hydrolysis of the halogen compounds.

OXIDATION PRODUCTS OF ETHYL ALCOHOL.  
(Compare § 75).

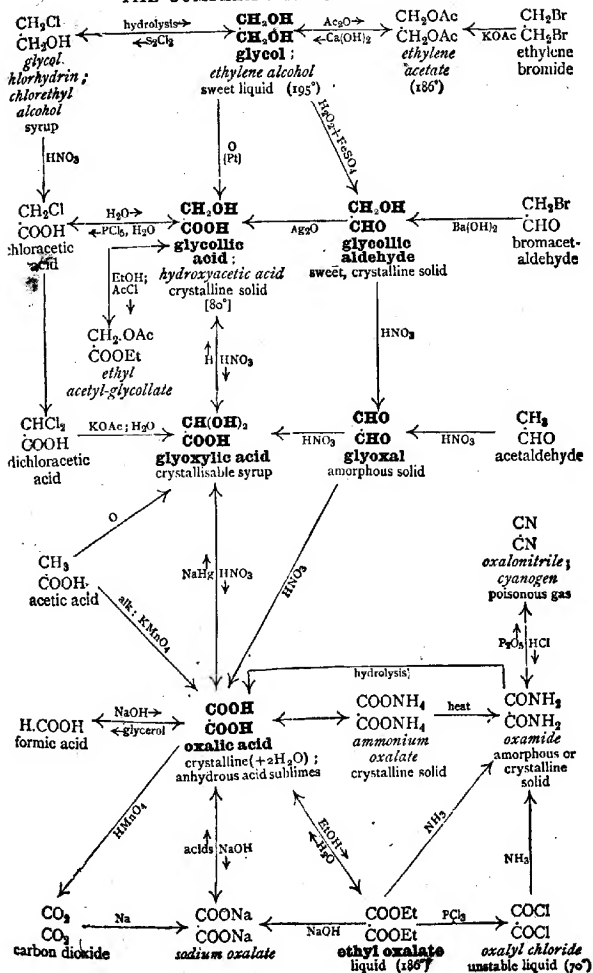


(1) Acetaldehyde,  $\text{CH}_3.\text{CHO}$ . (2) Glycol,  $\text{CH}_2\text{OH}.\text{CH}_2\text{OH}$ . (3) Acetic acid,  $\text{CH}_3.\text{COOH}$ . (4) Glycollic aldehyde,  $\text{CH}_2\text{OH}.\text{CHO}$ . (5) Glycollic acid,  $\text{CH}_2\text{OH}.\text{COOH}$ . (6) Glyoxal,  $\text{CHO}.\text{CHO}$ . (7) Glyoxylic acid,  $\text{CHO}.\text{COOH}$ . (8) Oxalic acid,  $\text{COOH}.\text{COOH}$ .

The existence of this extensive series affords a very striking demonstration of the validity of the theory of structure and valency.

**126. Synopsis.**—Corresponding with the halogen substitution products of the ethyl-acetic series, there is a series of hydroxy-derivatives, comprising alcohols, aldehydes, acids, and compounds in which these functions are united in pairs. The chief of these doubly-functioned compounds are the diprimary alcohol glycol, and the dicarboxylic acid oxalic acid.

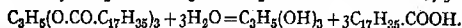
## THE COMPLEX HYDROXY-ETHANES.



SECTION VII  
THREE-CARBON DERIVATIVES  
CHAPTER XXIII

THE GLYCEROL-MESOXALIC SERIES

127. **Glycerol.**—The alcohol, glycerol, with which the acids are combined in the natural fats, is a trihydroxy-propane, analogous to glycol. It is obtained by distilling with superheated steam the alkaline lye which remains after the saponification of fat; the glycerol vapour mixes with the steam, and is carried over and condensed with it, and on evaporating the distillate at a low temperature, is left as a syrupy liquid. It is dried by simple heating in an open vessel at about 175°.



The hydrolysis is also readily effected by boiling the fat with litharge and water, the resulting solution being simply filtered from the insoluble lead soap; glycerol was originally obtained from olive oil in this way. Commercially glycerol is prepared by direct hydrolysis of fat with sulphuric acid and isolated by distillation with superheated steam.

*Glycerol* or *glycerine*,  $\text{CH}_2\text{OH}.\text{CHOH}.\text{CH}_2\text{OH}$  (Scheele, 1779; γλυκὺς=sweet, κηρός=wax), is a sweet, viscid liquid, which boils at 290°, without undergoing decomposition when pure; the specific gravity of the liquid is 1.28 at 20°, and it freezes at a low temperature to a crystalline solid, melting at 20°.

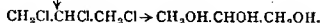
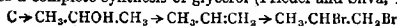
The molecular formula of glycerol is  $\text{C}_3\text{H}_8\text{O}_3$ . The presence of three alkylic hydroxyl groups is shown by the formation of mono-, di- and tri-acetyl derivatives (§ 128), and it is thus a tri-acid alcohol of the formula  $\text{C}_3\text{H}_5(\text{OH})_3$ . By heating with hydriodic acid and phosphorus it is reduced to propane, of which it is thus the trihydroxide (Berthelot, 1854), and as it is a stable compound, and can be distilled unchanged, the

three hydroxyl groups must be attached to separate carbon atoms (compare Chloral and Orthoacetic Acid, §§ 115, 77).

Glycerol is therefore represented by the constitutional formula—



This is confirmed by its behaviour on oxidation (§ 129), and by its synthesis from isopropyl alcohol. The latter alcohol is converted into propylene and propylene dibromide in the manner already described, (§ 106), and the dibromide is converted into trichloropropane by energetic chlorination in presence of iodine, bromine and hydrogen alike being replaced by chlorine. This chloro-paraffin is identical with trichlorhydrin, the trichloro-derivative of glycerol (§ 128), and is readily hydrolysed to glycerol by heating with silver oxide and water. As isopropyl alcohol can be made from acetone, and thus from acetic acid and carbon, this constitutes a complete synthesis of glycerol (Friedel and Silva, 1873).



**128. Ethereal Salts of Glycerol: the Glycerides.**—The ethereal salts of glycerol are sometimes distinguished by the suffix *-in*. The hydrochloric acid salts or *chlorhydrins* are viscid or mobile liquids, according to the proportion of chlorine, and like the acetates are readily hydrolysed to glycerol.

Mono- and di-chlorhydrin each exist in two isomeric forms, differing in the position of the chlorine. The  $\alpha$ -modifications, in which the secondary alcohol group is unaltered, may be formed by direct action of hydrochloric acid, but  $\alpha$ -dichlorhydrin is best made by the action of sulphur "monochloride." The perfectly dry glycerol is heated on a water-bath with the mono-chloride until hydrochloric acid ceases to be evolved. The dichlorhydrin is extracted from the product with ether, in which it is freely soluble, and the insoluble ethereal solution is separated with a tap-funnel and fractionated.



*$\alpha$ -Dichlorhydrin*,  $\text{CH}_2\text{Cl.CH(OH).CH}_2\text{Cl}$  (Berthelot, 1854), is a colourless ethereal liquid, boiling at  $176^\circ$ ; it is reduced to isopropyl alcohol by sodium amalgam, and oxidised to *dichloroacetone*,  $\text{CH}_2\text{Cl.CO.CH}_2\text{Cl}$ , by chromic acid, whence its constitution; it is an important stepping-stone in the synthesis of citric acid (§ 165). By the action of phosphorus pentachloride, both dichlorhydrins are converted into the corresponding *trichlorhydrin* or *trichloropropane*,  $\text{CH}_2\text{Cl.CHCl.CH}_2\text{Cl}$ , which is a mobile liquid resembling chloroform, and boiling at  $158^\circ$ .

The chlorhydrins form internal ethers analogous to ethylene oxide. When, for example,  $\alpha$ -dichlorhydrin is slowly poured into concentrated caustic soda, a vigorous action takes place in the same way as with glycol chlorhydrin, and *epi-chlorhydrin* passes over.



*Epichlorhydrin*,  $\begin{array}{c} \text{—O—} \\ | \\ \text{CH}_2\text{—CH} \end{array} \text{CH}_2\text{Cl}$  (Berthelot), is an oily (thereal liquid, boiling at  $117^\circ$ . Like ethylene oxide, it readily unites with hydrochloric acid, and is reconverted into the dichlorhydrin. The corresponding alcohol, *glycide alcohol*,  $\begin{array}{c} \text{—O—} \\ | \\ \text{CH}_2\text{—CH} \end{array} \text{CH}_2\text{OH}$ , a liquid boiling at  $162^\circ$ , is obtained by the action of potash on  $\alpha$ -monochlorhydrin; it resembles glycerol, and is easily hydrated to it.

Glycerol nitrate, which is formed by adding glycerol slowly to a well-cooled mixture of concentrated nitric and sulphuric acids, is the well-known explosive "nitroglycerine." On pouring the solution thus obtained into a quantity of cold water, the nitrate separates as a heavy oil, which is washed until free from acid, and dried with calcium chloride.

*Glycerol trinitrate* or *trinitrin*,  $\text{C}_3\text{H}_5(\text{O}.\text{NO}_2)_3$  (Sobrero, 1847), is a colourless oil, which is sweet in taste, but poisonous, even when absorbed through the skin. Although it burns quietly in an open vessel, it explodes with great violence when struck or suddenly heated. On account of its uncertain behaviour, and for convenience in transport, nitro-glycerine is usually mixed with three times its weight of an absorbent siliceous earth, and in this form is known as *dynamite* (Nobel).

Explosive substances, such as glycerol trinitrate, cannot be analysed by the usual methods; as a general rule, the compound is sealed up in a hard glass tube with excess of copper oxide, and the tube embedded in plaster of Paris and heated to redness; the explosion is confined to the tube, so that the gaseous products can be drawn off and analysed.

The three acetates or *acetins* already mentioned are viscid liquids of high boiling point; they are formed by heating glycerol with glacial acetic acid or acetic anhydride, the number of acetyl groups entering into combination depending on the temperature and proportions. *Mono-* and *di-formin* are similar substances; the latter is an oily liquid which can be extracted with ether from the residue obtained in the preparation of formic acid from glycerol and anhydrous oxalic acid; when heated with anhydrous oxalic acid it yields formic acid and carbon dioxide. The tributyrates or *tributyryns* is the ethereal salt in which the butyric acid exists in butter fat.

The salts of glycerol with Organic acids are sometimes termed the *glycerides*. The common fats are glycerides of the fatty and related acids,\* and can in some cases be made by direct synthesis. *Stearin* or *glycerol tristearate*,  $\text{C}_3\text{H}_5(\text{O}.\text{CO}.\text{C}_{17}\text{H}_{35})_3$ , which can be isolated from mutton fat by fractional crystallisation from ether, is also formed by heating stearic acid with glycerol at a high temperature; the product

\* Lanolin, or wool fat, however, which is distinguished by its property of passing through the skin, is a mixture of the fatty acid esters of *cholesterol*,  $\text{C}_{26}\text{H}_{43}.\text{OH}$ , a crystalline aliphatic alcohol, which also occurs in the free state in red blood corpuscles.

from either source crystallises in lustrous plates, melting at  $66^{\circ}$ . All three palmitins and triolein (§ 48) have been synthesised in the same way.

**129. Oxidation Products of Glycerol.**—As glycerol contains a secondary alcohol group in addition to the two primary groups of glycol, it is obvious that its oxidation products must be more complex (compare § 125). The majority of these oxidation products are known (see Scheme), the most important being glyceraldehyde, glyceric acid and mesoxalic acid.

Glyceraldehyde or glycerose is readily prepared by oxidising glycerol with hydrogen peroxide in presence of ferrous sulphate (Fenton, 1899).

The diluted glycerol is mixed with some fresh ferrous sulphate solution and concentrated hydrogen peroxide is slowly added, the rapid rise in temperature being moderated by immersing the vessel in cold water. When the reaction is over, the cooled product is well shaken with freshly precipitated barium carbonate to remove the iron and sulphuric acid, and the clear filtrate containing the glycerose is evaporated under diminished pressure (*i.e.* at a comparatively low temperature).

*Glycerose* or *glyceric aldehyde*,  $\text{CH}_2\text{OH}.\text{CHOH}.\text{CHO}$ , is a sweet syrup, which resembles glycollic aldehyde in all its actions. Like the lower aldehyde it is polymeric with formaldehyde, and is convertible into more complex aldehydes (sugars) by further polymerisation (§ 188).

Like all aldehydes, glycerinaldehyde is oxidised by silver oxide to the corresponding acid, glyceric acid; this is better prepared, however, by direct oxidation of glycerol with diluted nitric acid.

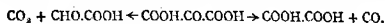
A mixture of glycerol and water is placed in a tall narrow cylinder, and a layer of fuming nitric acid introduced beneath it by means of a thistle funnel; at the end of a week the nitric acid has inter-diffused with and oxidised the glycerol, and the product is then evaporated to a syrup on a water bath. The crude glyceric acid is diluted and boiled with calcium carbonate, and the recrystallised calcium salt is suspended in water and decomposed with oxalic acid; on evaporating the clear liquid the glyceric acid remains as a syrup.

*Glyceric* or *dihydroxypropionic acid*,  $\text{CH}_2\text{OH}.\text{CHOH}.\text{COOH}$  (Debus, 1858), is a syrupy acid liquid, which has not been made to crystallise; it is converted by phosphorus diiodide into  $\beta$ -iodopropionic acid (§ 132).

The theoretical end product of the limited oxidation of glycerol, mesoxalic acid, can only be obtained from it by indirect processes, as it is not stable. It is prepared by hydrolysis of allozan, an oxidation product of uric acid (195), with baryta water, the resulting barium mesoxalate being decomposed with dilute sulphuric acid.

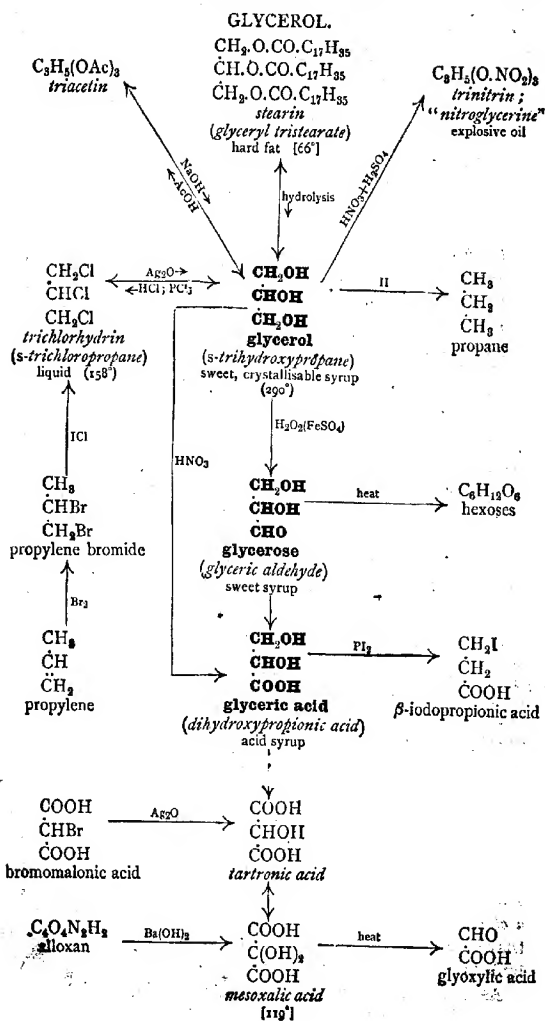


*Mesoxalic acid*,  $\text{COOH.CO.COOH} + \text{H}_2\text{O}$  (Liebig and Wöhler, 1838), is a crystalline substance, melting at  $119^\circ$ . It loses its water only with difficulty, so that the latter is possibly combined in hydroxylic form with the ketonic group, in the same way as in chloral hydrate. As a ketone the acid forms a *phenylhydrazone*, a yellow crystalline substance melting at  $164^\circ$ ; it is reduced by sodium amalgam to the corresponding secondary alcohol, *tartronic acid*,  $\text{COOH.CHOH.COOH}$ , a similar crystalline substance, which may also be prepared by the action of silver oxide on bromomalonic acid,  $\text{COOH.CHBr.COOH}$  (see § 148), or by boiling dihydroxy-tartaric acid (§ 160) with water. When mesoxalic acid is heated, it is decomposed into carbon dioxide and glyoxylic acid, whilst by evaporating its aqueous solution it is largely resolved into carbon monoxide and oxalic acid.



By dehydration, or dehydration and reduction, glycerol is convertible into olefinic derivatives, which are considered in the following chapter.

**130. Synopsis.**—Glycerol is a trihydroxy-propane analogous to glycol, and its ethereal salts with the fatty acids constitute the ordinary fats. It is prepared from the latter by saponification or hydrolysis, and can also be made from its elements.

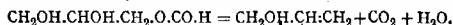


## CHAPTER XXIV

### THE UNSATURATED ALCOHOLS AND ACIDS

**131. Allyl Alcohol and its Derivatives.**—Before passing to the remaining oxygenated derivatives of propane, some compounds related to propylene and other unsaturated hydrocarbons must be considered. The primary alcohol derived from propylene is termed allyl alcohol, its sulphide, prepared by distilling allyl iodide with potassium sulphide, being identical with the oil which is obtained by distilling garlic (*allium*) with steam (Wertheim, 1844).

Allyl alcohol is easily made by reducing glycerol with formic acid (Tollens, 1870). If in the preparation of this acid from oxalic acid and glycerol the heating is continued after distillation has ceased, the evolution of carbon dioxide recommences, owing to decomposition of the monoformin (§ 128); oily drops of the unsaturated alcohol then begin to run down the sides of the flask, and presently distil over.



The portion of the liquid which distils whilst the temperature of the reacting mass is rising from 190° to 260° is saturated with solid caustic potash, and left in contact with excess of this agent for some days, by which time all the acrolein and water, as well as the formic acid, have been eliminated. Finally the whole product is distilled from an oil-bath, and on redistillation is pure.

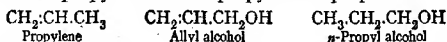
The yield is increased by adding a trace of ammonium chloride, in order to convert the small quantity of sodium oxalate, which is usually present, into the ammonium salt.

*Allyl alcohol*,  $\text{CH}_2\text{CH}.\text{CH}_2\text{OH}$  (Cahours and Hofmann, 1857), is a colourless pungent liquid, which boils at 97°, freezes at -90°, and has a specific gravity of 0.871 at 0°. The presence of alkylic hydroxyl is proved by the formation of an *acetate*, when the alcohol is mixed with acetyl chloride, and that of the primary alcohol group by its oxidation to an aldehyde and acid containing the same number of carbon atoms.

As the molecular formula of allyl alcohol is  $\text{C}_3\text{H}_6\text{O}$  (also

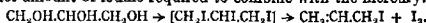
that of acetone), this result leads to a rational formula,  $C_2H_3.CH_2OH$ , containing the unsaturated vinyl radical,  $C_2H_3$ ; the alcohol is therefore an unsaturated compound, and presumably an ethylene derivative.

The presence of an ethylene linkage is finally established by the instant decolorisation of bromine water, and reduction of cold, dilute, alkaline permanganate by the liquid. Allyl alcohol is thus hydroxy-propylene, and bears the same relation to propyl alcohol as propylene to propane.

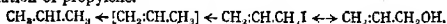


Allyl iodide is readily prepared from glycerol by the action of iodine and phosphorus. Yellow phosphorus, in small pieces, is slowly added to a mixture of dry glycerol and powdered iodine, air being excluded by a slow stream of carbon dioxide; there is a brisk action after each addition of phosphorus, and the iodide at once distils off, gentle heat being applied if necessary. Isopropyl iodide is formed if water is added. On redistilling the dried heavy layer of allyl iodide, it passes over within two or three degrees of its boiling point, and is fairly pure.

To completely eliminate the isopropyl iodide, the product is shaken with alcohol and metallic mercury, with which the unsaturated iodide forms a crystalline, additive *mercury compound*,  $C_3H_5HgI$ ; this is recrystallised from hot alcohol, and decomposed by shaking the still moist crystals with the exact amount of iodine required to combine with the mercury.

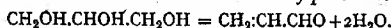


*Allyl iodide*,  $CH_2:CH.CH_2I$  (Berthelot, 1854), is a heavy colourless liquid, which boils at  $101^\circ$ , and has a pronounced odour of garlic. Its constitution is established by its relation to allyl alcohol, into which it is converted by warming with lead oxide and water, and from which it is formed by the action of phosphorus and iodine. When warmed with hydriodic acid, it is converted into isopropyl iodide, owing probably to the intermediate formation of propylene.



The first allyl compound obtained was the isothiocyanate or oil of mustard (Lefebvre, 1660, § 210).

**132. Acrolein and Acrylic Acid : Crotonic Acids.**—The aldehyde formed by oxidising allyl alcohol with chromic acid is conveniently made by dehydrating glycerol, by heating with twice its weight of acid potassium sulphate. The distillate obtained from well-dried materials is nearly pure acrolein.



*Acrylic aldehyde* or *acrolein*,  $CH_2:CH.CHO$  (Redtenbacher, 1843), is a mobile liquid, which boils at  $52^\circ$ , and is intolerably pungent and irritating in odour; it is very unstable, and soon polymerises spontaneously to a white translucent solid, *dis-acryl*, resembling porcelain. As an aldehyde, acrolein reduces

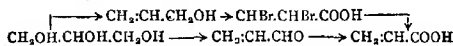
silver, colours bleached rosaniline, and is resinified by caustic soda, etc.; it is easily reduced to allyl alcohol by zinc and dilute hydrochloric acid, and is oxidised by silver oxide to the corresponding acid, acrylic acid. As an ethylene derivative it combines directly with bromine.

The additive compound, *acrolein dibromide*,  $\text{CH}_2\text{Br}.\text{CHBr}.\text{CHO}$ , is converted by ice-cold baryta water into inactive fructose (§ 187), a sugar which is closely related to and convertible into some of the natural sugars.

When acrolein-ammonia is distilled with phosphorus pentoxide, it is converted into picoline (§ 352), a basic substance closely related to the vegetable alkaloids.

Acrolein is readily oxidised to acrylic acid. The aqueous solution is digested with silver oxide in the dark; the product is then boiled, and the silver precipitated from the resulting silver acrylate with sodium carbonate; the sodium acrylate is distilled with dilute sulphuric acid, and the pure acid obtained by decomposing the dry lead salt with hydrogen sulphide.

Anhydrous acrylic acid may also be prepared by the action of reduced copper, containing a little iron, on *α,β-dibromopropionic acid*,  $\text{CH}_2\text{Br}.\text{CHBr}.\text{COOH}$ , a crystalline substance which is readily obtained by oxidising allyl alcohol dibromide.



*Acrylic acid*,  $\text{CH}_2\text{CH}.\text{COOH}$  (Redtenbacher, 1843), is a liquid which closely resembles acetic acid in appearance and odour, but is easily distinguished from the saturated fatty acid by instantly decolorising bromine; it boils at  $141^\circ$ , and readily freezes to an ice-like solid, melting at  $10^\circ$ .

Acrylic acid is a distinctly stronger acid than acetic or propionic acid, its dissociation constant being  $K = 0.0056$ ; the loss of two hydrogen atoms thus converts the positive ethyl group into the slightly electronegative vinyl group; the acid is therefore more reactive than propionic acid in two ways: it is a stronger acid, and it is an unsaturated compound (compare Propionic Acid, § 134). As an acid, acrylic acid forms the usual salts, but its ethereal salts can only be made indirectly, owing to the reactivity of the unsaturated radical with the ordinary esterifying agents.

As an ethylene derivative it unites directly with bromine, forming the above dibromopropionic acid; and for the same reason it is oxidised by dilute alkaline permanganate to glyceric acid, a hydroxyl group being added in the normal manner to each of the ethylene carbon atoms; when boiled with zinc and dilute hydrochloric acid, it is reduced to propionic acid.

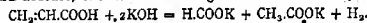
Acrylic acid also unites with hydriodic acid, forming *β-iodopropionic acid*,  $\text{CH}_2\text{I}.\text{CH}_2.\text{COOH}$ , a crystalline substance which is reconverted into the unsaturated acid by distillation with litharge. *β-Iodopropionic acid*



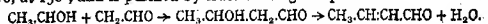
is also formed when phosphorus diiodide is mixed with glyceric acid; there is a violent action, and on heating the product it clears to a liquid which crystallises on cooling; the crude acid is recrystallised from hot light petroleum.



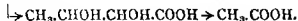
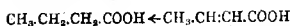
When acrylic acid is fused with caustic potash, it is oxidised to potassium formate and acetate, the molecule being broken at the ethylene linkage,



We have noted that one of the condensation products of acetaldehyde is an aldehydic substance, crotonaldehyde; this is readily formed by heating aldehyde with zinc chloride and a few drops of water, for a day or two, at  $150^\circ$ , and is purified by fractionating the product.



*Crotonaldehyde*,  $\text{CH}_3.\text{CH}:\text{CH}.\text{CHO}$ , is a liquid which resembles acrolein, but boils at  $105^\circ$ . It is converted by silver oxide into the corresponding *crotonic acid*,  $\text{CH}_3.\text{CH}:\text{CH}.\text{COOH}$ , a crystalline substance of butyric odour, melting at  $72^\circ$ . Crotonic acid is also formed when  $\beta$ -hydroxybutyric acid (§ 143) is distilled with sulphuric acid; its constitution follows from its reduction to normal butyric acid by zinc and acid, and its conversion by dilute alkaline permanganate into the alkali salt of *dihydroxybutyric acid*; this acid yields acetic acid when further oxidised and is thus a methyl compound.



There is a second crotonic acid of precisely the same constitution, the existence of which, and other similar compounds, has led to a further development of the theory of structure (§ 155).

**133. The Acrylic Series: Oleic Acid.**—The most important of the higher members of the acrylic series is oleic acid, a compound which bears the same relation to stearic acid as acrylic to propionic acid. Its glycerol salt, *triolein*, is readily separated from olive or almond oil by cooling with ice; the bulk of the accompanying stearin and palmitin crystallises out at once, and the remainder separates on diluting the residual oil with alcohol and again cooling; the alcohol is then distilled off, and the olein fractionated under low pressure (§ 143).

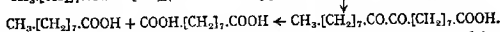
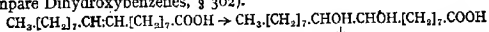
Oleic acid is prepared by boiling crude triolein with lead oxide and water, and extracting the lead oleate from the mixed lead soaps with ether, in which it is freely soluble; the lead is precipitated from the ethereal solution with hydrochloric acid, and the acid is left in a fairly pure state on evaporating the filtrate.

*Oleic acid*,  $\text{CH}_3.[\text{CH}_2]_7.\text{CH}:\text{CH}.[\text{CH}_2]_7.\text{COOH}$  (Chevreul, 1811), is a colourless, odourless oil, which solidifies at a low temperature to a crystalline solid melting at  $14^\circ$ ; it is reduced by

hydriodic acid and phosphorus at  $200^{\circ}$  to stearic acid, whence its normal constitution, and is oxidised by fusion with potash to potassium palmitate and acetate.

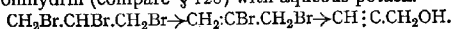
As an ethylene derivative, oleic acid decolorises bromine, forming an oily additive compound,  *dibromostearic acid* , and it is oxidised by dilute alkaline permanganate in the normal manner to the corresponding hydroxy-compound or glycol,  *dihydroxystearic acid* ,  $C_{17}H_{33}(OH)_2COOH$  (Saytzeff, 1885), a crystalline substance melting at  $134^{\circ}$ .

This dihydroxy-acid is resolved by further oxidation into two nine-carbon acids:  *pelargonic acid* ,  $C_9H_{17}COOH$ , a normal fatty acid boiling at  $254^{\circ}$ , and  *azelaic acid* ,  $COOH.C_7H_{14}.COOH$ , a normal homologue of oxalic acid, melting at  $106^{\circ}$ ; the hydroxyl groups, and thus the ethylene linkage are therefore at the centre of the molecule. Fusion with potash often causes molecular transposition, and is valueless as a test of constitution (compare Dihydroxybenzenes, § 302).



When oleic acid is treated with nitrous anhydride, it is converted into  *elaidic acid* , a crystalline solid which melts at  $45^{\circ}$ , but has exactly the same constitution (compare § 155).

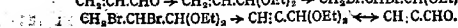
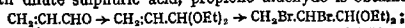
**134. Propargyl Alcohol: Propiolic Aldehyde and Acid.**—Only one alcohol of the acetylene series is known, namely propargyl alcohol, which is formed by heating bromallyl bromide with alcoholic potash; the bromallyl bromide is made by heating tribromhydrin (compare § 128) with aqueous potash.



*Propargyl alcohol* ,  $CH:C.CH_2OH$  (Henry, 1878), is a liquid of pleasant odour, boiling at  $115^{\circ}$ . As an alcohol it forms esters, such as  *propargyl bromide* ,  $CH:C.CH_2Br$ , and  *propargyl acetate* ; whilst as an acetylene derivative it yields metallic compounds such as the  *cuprous compound* ,  $Cu_2(C:C.CH_2OH)_2$ , an explosive yellow solid. The esters of propargyl alcohol also form metallic compounds.

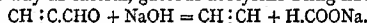
The aldehyde corresponding with propargyl alcohol is prepared by a similar process from the acetal of acrolein dibromide.

This compound is converted by alcoholic potash into  *propiolic acetal* ,  $CH:C.CH(OEt)_2$ , a stable liquid boiling at  $141^{\circ}$ , and on hydrolysing this acetal with dilute sulphuric acid, propiolic aldehyde is obtained.



*Propiolic aldehyde* ,  $CH:C.CHO$  (Claisen, 1898), is a liquid of intensely irritating odour, boiling at  $61^{\circ}$ ; it resembles acrolein

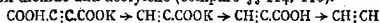
in its general actions, and as an acetylene derivative forms metallic compounds. The acetylenyl group is so intensely negative that propiolic aldehyde is hydrolysed by alkalis in the same way as chloral, gaseous acetylene being liberated.



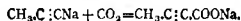
The potassium salt of the corresponding acid is obtained when the acid potassium salt of acetylene-dicarboxylic acid,  $\text{COOH}.\text{C}:\text{C}.\text{COOK}$  (§ 156), is heated with water.

*Propiolic acid*,  $\text{CH}:\text{C}.\text{COOH}$  (Bandrowski, 1880), is a liquid resembling acrylic and acetic acids; it boils at  $144^\circ$ , and solidifies in the cold to silky crystals melting at  $6^\circ$ .

Owing to the electronegative character of the acetylenyl radical, propiolic acid is a very powerful acid, and readily forms esters such as *ethyl propiolate*,  $\text{CH}:\text{C}.\text{COOEt}$ , a liquid boiling at  $112^\circ$ . As an acetylene derivative it yields explosive *silver* and *copper* compounds; it is reduced to acrylic acid by sodium amalgam, and by prolonged boiling with water is converted into carbon dioxide and acetylene (compare §§ 114, 116).



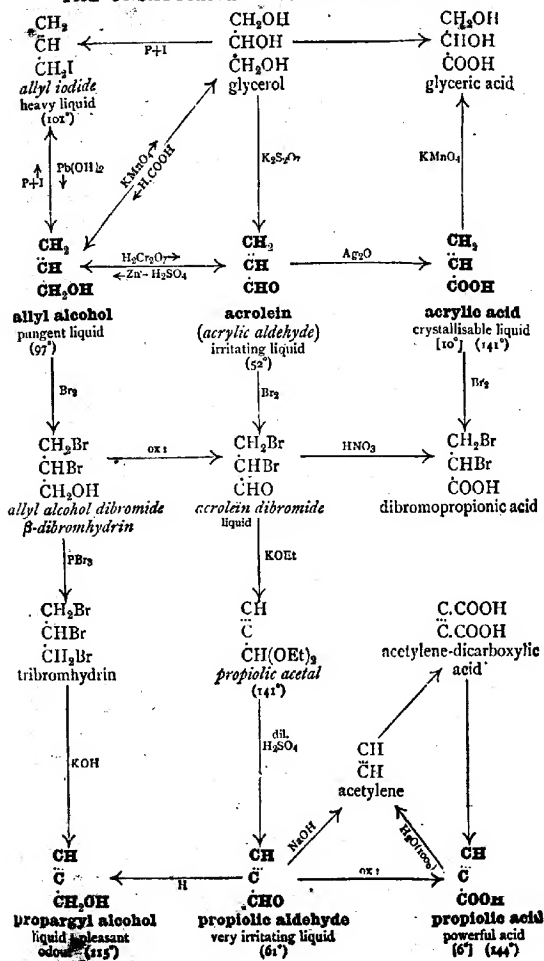
Several homologues of propiolic acid are known. The sodium salt of *tetrolic acid*,  $\text{CH}_3.\text{C}:\text{C}.\text{COONa}$ , is formed by direct combination of sodium allene with carbon dioxide in ether. Like allene, tetrolic acid does not form metallic compounds; it is reduced to crotonic acid by sodium amalgam.



*Sorbic acid*,  $\text{CH}_3.\text{CH}:\text{CH}.\text{CH}:\text{CH}.\text{COOH}$ , a crystalline compound melting at  $134^\circ$ , occurs naturally in the unripe berries of the mountain ash, and can be prepared synthetically from crotonaldehyde and malonic acid (§ 148); it is a diolefinic compound, and not a true homologue of propiolic acid. *Linoleic acid*,  $\text{C}_{17}\text{H}_{31}.\text{COOH}$ , is the active constituent of linseed and other "drying" oils; the liquid acid and its glycerides and salts oxidise with great rapidity to solid resinous substances; hence when paint is made with linseed oil it rapidly becomes dry and hard.

**185. Synopsis.**—The higher olefines and acetylenes are connected with alcohols and acids, which are similar to the paraffin alcohols and acids, but unsaturated. Allyl alcohol and acrylic acid are typical members of the first class, and propargyl alcohol and propiolic acid of the second.

## THE UNSATURATED ALCOHOLS AND ACIDS.



## CHAPTER XXV

### THE FOUR LACTIC ACIDS : STEREOISOMERISM

**136. Fermentation Lactic Acid.**—When milk turns sour, the milk-sugar is converted by a microscopic fungus, *bacillus lacti*, into lactic acid, a compound which bears the same relation to propionic acid as glycollic to acetic acid ; it is conveniently prepared from cane-sugar by a similar fermentation.

The sugar is dissolved in water and acidified with tartaric acid, and after a few days sour skim milk and a little putrid cheese are added, to provide and nourish the ferment. At the same time, zinc carbonate is stirred in to neutralise the acid as it is formed, which would otherwise stop the action. The mixture is kept warm for a week, and frequently stirred, and on boiling and filtering the semi-solid product, zinc lactate crystallises out.\*

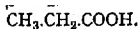
The free acid is obtained by decomposing the zinc salt, suspended in water, with sulphuretted hydrogen. The filtered solution is concentrated, and the lactic acid separated from admixed mannitol (§ 132) by extraction with ether, in which the mannitol is insoluble.

Lactic acid is also formed by heating various sugars with caustic alkali. Thus when invert sugar (§ 169) is heated with strong caustic soda solution for some hours at a moderate temperature, the solution loses the characteristic reducing properties due to the sugar, and after neutralising the alkali lactic acid can be separated by means of its zinc salt (Hoppe-Seyler, 1871). It is also formed synthetically in various ways ; and was first synthesised by the action of nitrous acid on alanine (Strecker, 1848, § 220).

*Fermentation or inactive lactic acid*,  $\text{CH}_3\cdot\text{CHOH}\cdot\text{COOH}$  (Scheele, 1780), is a syrupy liquid, having a specific gravity of 1.248 at 15° ; it is decomposed when distilled under ordinary pressure, but when fractionated under the lowest pressure of a mercury pump (0.5–1 mm.) distils unchanged at about 85°,

\* If the fermentation be continued, the lactate is converted by a second ferment into the butyrate, with evolution of hydrogen and carbon-dioxide. For this purpose calcium carbonate is better than the zinc salt. The mass eventually becomes liquid, and as soon as the evolution of gas has ceased, the lime is precipitated with washing soda solution, and the sodium butyrate decomposed with dilute sulphuric acid.

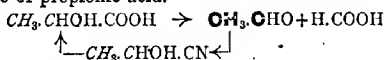




The  $\alpha$ -constitution is decisively established by the interconvertibility of the acid with acetaldehyde. When lactic acid is heated with dilute sulphuric acid in a sealed tube at  $120^\circ$ , it is hydrolysed to aldehyde and formic acid. Conversely, it is itself formed when aldehyde hydrocyanide is hydrolysed (Wislicenus, 1863).

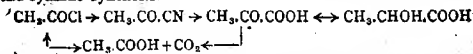
If a mixture of aldehyde with concentrated hydrocyanic and hydrochloric acids be kept until ammonium chloride ceases to separate, lactic acid is produced almost quantitatively, and can be extracted from the product with ether.

As the acid is interconvertible with acetaldehyde, it must contain the ethylidene nucleus of this substance; hence the methyl or  $\beta$ -group is intact, and lactic acid is the  $\alpha$ -hydroxy-derivative of propionic acid.

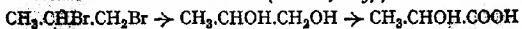


The constitution of lactic acid as a secondary alcohol (the  $\beta$ -acid is a primary alcohol) is further indicated by its oxidation by dilute permanganate to the corresponding ketonic acid, pyroracemic acid, and its formation from this acid by reduction with zinc-dust and water.

*Pyroracemic* or *pyruvic acid*,  $\text{CH}_3\text{CO.COOH}$ , which is readily prepared by distilling racemic or tartaric acid (§ 159) with potassium pyrosulphate is a liquid which boils at  $168^\circ$ , freezes at  $9^\circ$ , and smells like acetic acid; its dissociation constant is  $K = 0.56$ , so that the substitution of oxygen for two atoms of hydrogen increases the acidity of propionic acid more than three-hundredfold. As a ketone, pyroracemic acid forms a *phenylhydrazone*, an insoluble, yellow crystalline substance melting at  $192^\circ$ ; and when oxidised it is resolved, in the normal ketonic manner, into acetic acid and carbon dioxide; its constitution is confirmed by its formation from acetyl chloride by the cyanide synthesis.

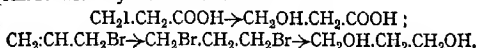


Lactic acid is also formed by oxidising *propylene glycol* with air in presence of platinum black; its molecular weight was first established in this manner (Wurtz, 1857).



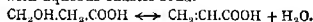
**183. Hydracrylic Acid.**—The second hydroxy-propionic or *acrylene-lactic acid*, is prepared by warming  $\beta$ -iodopropionic acid (§ 132) with silver oxide and water, and evaporating the product in a vacuum over sulphuric acid. It is also formed by oxidising  $\beta$ -propylene or trimethylene glycol, which is made

from the trimethylene bromide prepared by direct union of allyl bromide with hydrobromic acid.

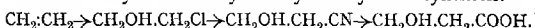


*Hydracrylic* or *ethylene-lactic acid*,  $\text{CH}_2\text{OH}.\text{CH}_2.\text{COOH}$  (Wislicenus, 1863), is a syrupy liquid resembling ordinary lactic acid.

Its dissociation constant is  $K = 0.0031$ , so that the introduction of a hydroxyl group in the  $\beta$ -position only slightly increases the acidity of propionic acid. As an alcohol-acid, hydracrylic acid is converted by phosphorus pentachloride into an alkyl-acid chloride,  *$\beta$ -chloropropionyl chloride*, but it differs from ethylidene-lactic acid in that it is converted by oxidising agents into carbon dioxide and oxalic acid. It is resolved, moreover, by distillation, not into an internal ethereal salt like lactide, but into acrylic acid and water; conversely acrylic acid is converted into sodium  $\beta$ -lactate by simply boiling with aqueous caustic soda.



The constitution of  $\beta$ -lactic acid is confirmed by its formation from ethylene chlorhydrin by the cyanide synthesis.



**139. The Active Lactic Acids : Optical Activity.**—Although according to the theory of structure there should be two hydroxypropionic acids, and only two, there are actually four. The third, or *sarcosolactic acid*, is found in muscle, and therefore in extract of meat, from which it is isolated by precipitating the albumen, etc., with alcohol, and extracting the acidified, alcohol-free filtrate with ether (Liebig, 1847).

*Sarcosolactic acid*,  $\text{CH}_3.\text{CHOH}.\text{COOH}$  (Berzelius, 1808), is a syrup, which resembles fermentation lactic acid in almost every respect; all its actions show that it is  $\alpha$ -hydroxy-propionic acid. With the exception of the solubilities of their salts (*zinc sarcosolactate*, for example, is more soluble than the corresponding salt of fermentation lactic acid), the two acids are chemically identical.

Physically, however, they differ widely, for whilst fermentation lactic acid is without action on polarised light, *sarcosolactic acid* rotates the plane of polarisation of such light in a positive direction, or, as it is termed, is optically active, and dextrorotate;  $[\alpha]_D = +3.5^\circ$ .

The rotation of the plane of polarisation by an optically active substance is proportional to the thickness of the layer traversed by the light, and to the strength of the solution, and is usually expressed in terms of the specific rotatory power, i.e. the rotation which would be caused by a layer 10 cm. thick of a solution containing 1 gram of the substance per cc. The specific



rotatory power is denoted by the symbol  $[\alpha]_D$  (sodium light being used), and is constant for each substance, provided that the temperature and concentration are constant.

$$[\alpha]_D = \frac{\text{actual rotation}}{\text{thickness of layer in dcm.} \times \text{grams of active substance per cc.}}$$

In a measurement of the rotatory power of sarcosolactic acid

7 grams were made up to 50 cc. at 15°.

The polarimeter having been adjusted to zero, and a 2-decimetre tube filled with the solution, the analysing prism had to be rotated + 0.95°.

to produce the same appearance of the field. Hence the specific rotatory power was

$$[\alpha]_D = \frac{+0.95 \times 50}{2 \times 7} = +3.4^\circ.$$

The optical activity of a substance is sometimes expressed in terms of its molecular rotation

$$[M]_D = \frac{[\alpha]_D \times m}{100},$$

i.e. the rotation which would be produced by 10 cm. of a solution containing 1 centigram-molecule per cc. ( $m$  = molecular weight).

Sarcosolactic acid can also be made by fermentation. When common mould, *penicillium glaucum*, is allowed to grow on a solution of ammonium lactate, ammonium sarcosolactate is formed; and by means of a special ferment, *micrococcus paralacti*, grape-sugar is directly convertible into sarcosolactic acid. But however the acid is prepared, its specific rotatory power is constant.

The fourth lactic acid (Schardinger, 1891) is formed by the action of *bacillus lævofacti* on cane-sugar. It resembles sarcosolactic acid in every respect, with the exception that it is lævogyrate, the specific rotary power being  $[\alpha]_D = -3.5^\circ$ . It is therefore termed *laevolactic*, or *l-lactic acid*, as distinguished from *dextrolactic* or *d-lactic acid*, and *inactive lactic* or *i-lactic acid*.

When dextrolactic and lævolactic acids are mixed in equal proportions, a product is obtained, which is not only inactive, but identical with fermentation lactic acid; similarly when equal weights of the easily soluble zinc salts of the optically active acids are dissolved together in warm water, the sparingly soluble inactive zinc lactate rapidly crystallises out (Schardinger, 1891).

Conversely, if a solution of the strychnine salt of inactive lactic acid be concentrated, the crystals which first appear consist of *strychnine lævolactate*, whilst the more soluble salt remaining in the solution is the corresponding dextrolactate (Purdie, 1892).

Strychnine (§ 462) is an optically active (lævogyrate) base, and as the rotatory power of a salt is the sum of the rotatory powers of the ions

composing it, strychnine *d*-lactate and *l*-lactate are not optically opposite. Hence they are not chemically identical, and their solubilities are different.

It is evident that fermentation lactic acid is either a mixture or a molecular compound of dextro- and lævo-lactic acids, and that all three have precisely the same constitution.

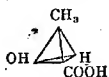
*d*-Lactic and *l*-lactic acids are termed optical antipodes, and *i*-lactic acid is said to be formed from them by external compensation (§ 163).

**140. The Asymmetrical Carbon Atom: Solid Formulæ.**—The difference between the three ethylidene lactic acids cannot be represented by means of ordinary structural formulæ. The common formula of the three acids differs, however, from that of hydracrylic acid, not only in the position of the hydroxyl group, but in that the central carbon atom is linked to four different groups and thus placed asymmetrically in the molecule.



Asymmetrical Structure of Lactic Acid.

Assuming that the four valencies are distributed around this central atom at equal angles in space, instead of in a plane, two solid formulæ become possible (Le Bel, Van't Hoff, 1874). The postulate is geometrically equivalent to representing the atom as a regular tetrahedron, to the apices of which the four groups are linked \* (Fig. 19).



Solid Formulæ of the Lactic Acids.

In both formulæ the four groups are linked to the central carbon atom, as in the plane formula, so that the structures are identical. Nevertheless, the formulæ are not identical; if the right hand be superposed on the left hand formula in such manner that the two methyl groups and the two carboxyl groups coincide, then the hydroxyl of the right hand falls over the hydrogen of the left hand formula, and *vice versa*.

The two solid formulæ are, in fact, mirror images of each other; the image of the left hand tetrahedron seen in the mirror is identical in appearance with the right hand tetrahedron, although the arrangement of the groups around the tetrahedra themselves is different. They are related, moreover, in the same way as the rotatory powers of the two

\* These formulæ are best studied from models. (See Appendix I.)

acids, for, looking from above, the sequence, H, OH, COOH, is clockwise in the right hand, and anticlockwise in the left-hand formula.

There is a further analogy, which although not yet proven in the case of the lactic acids, has been fully established in other similar cases (see Tartaric Acids, § 163). The crystals of optical isomerides are usually hemihedral, and the two kinds of crystals, like the two formulæ, are mirror images of each other, or enantiomorphous (*enantios* = opposite).

The active lactic acids are thus adequately represented by the single solid formulæ, and the inactive acid by the two together.

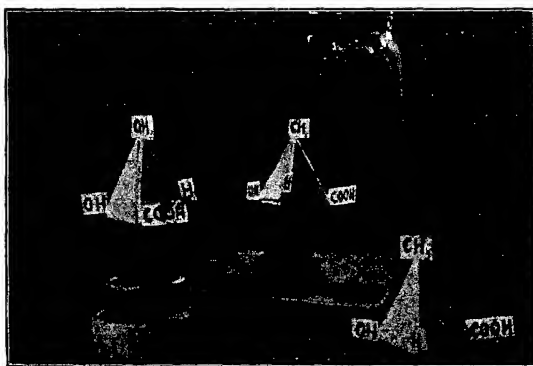


Fig. 19.—Stereoisomerism of the Lactic Acids.

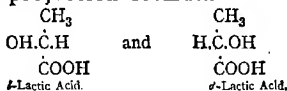
**141. Stereoisomerism.**—Such isomerism, representable only by solid formulæ, is termed stereoisomerism (*στερεος* = solid). All optically active substances contain asymmetrical nuclear atoms, and there is reason to believe that all compounds containing such asymmetrical atoms are either optically active themselves, or capable of resolution into optically active stereoisomerides.

Secondary-butyl carbinol,  $\text{CHMeEt}.\text{CH}_2\text{OH}$  (active amyl alcohol) and methylethylacetic acid,  $\text{CHMeEt}.\text{COOH}$  (active valeric acid) both contain asymmetrical carbon, and are both optically active. Glyceric acid,  $\text{CH}_2(\text{OH}).\text{CH}(\text{OH}).\text{COOH}$ , contains asymmetrical carbon, and can be resolved into optically active constituents.

Stereoisomerides have thus the same constitution and structure, and are said to differ in configuration. As the perspective views of the solid formulæ are rather cum-

142] *The Four Lactic Acids : Stereoisomerism* 181

brous, their plane projections are usually substituted, the solid formulæ of *l*-lactic and *d*-lactic acids being respectively represented by the projection formulæ—



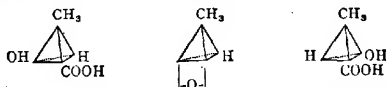
whilst the ordinary constitutional formula,  $\text{CH}_3 \cdot \text{CHOH} \cdot \text{COOH}$ , is reserved for the inactive or *dl*-acid.

If two of the attached groups or atoms become identical, the asymmetry and with it the optical activity, vanishes. Thus the lactic acids and glyceric acid are convertible into propionic acid, but the two projection formulæ



are identical, the corresponding solid formulæ superposable, and the products identical and inactive. The essential condition both for asymmetry and optical activity is the linking of four dissimilar groups to the central atom.

It is noteworthy that synthetic lactic acid is optically inactive, and this is almost invariably the case with synthetic compounds, for the chances of formation of the two asymmetrical configurations from symmetrical configurations are equal (compare § 163).



The phenomena of stereoisomerism were first studied in the tartaric acids (Pasteur, 1853).

**142. Synopsis.**—There are four hydroxypropionic acids, instead of the two required by the theory of structure, and three of these are structurally identical, but differ in their action on polarised light. As their molecules contain asymmetrical carbon, solid formulæ can be constructed for them which are identical in structure, but different in configuration or solid structure; the acids are therefore termed stereoisomerides.



## SECTION VIII

### FOUR-CARBON DERIVATIVES

#### CHAPTER XXVI

##### THE ACETOACETIC SYNTHESIS

**143. Ethyl Acetoacetate.**—Sodium dissolves readily in dry ethyl acetate, especially when warmed, hydrogen being evolved; the liquid becomes very alkaline, and eventually almost solid with a crystalline sodium compound. This compound is not directly derived from ethyl acetate, but from ethyl acetoacetate, a complex ester which is formed from it.

The ester is set free from the ethyl sodacetoacetate by adding excess of moderately concentrated acetic acid to the warm alkaline product, and after dissolving the resulting sodium acetate in a little water, is salted out with sodium chloride.

The crude ester is freed from alcohol and ethyl acetate by fractionation from a water-bath at as low a temperature as possible, and finally by fractionation under reduced pressure (Fig. 20); when pure it distils at about  $74^{\circ}$  under a pressure of 15 mm. The whole operation is conducted without a break, and as quickly as possible, because of the risk of hydrolysis; if too high a temperature be employed, much of the ester is converted into a crystalline substance, dehydracetic acid (§ 409). By cautious hydrolysis with cold, very dilute potash, ethyl acetoacetate is converted into potassium acetoacetate, from which the free acid may be liberated by cold, dilute sulphuric acid.

*Ethyl acetoacetate*,  $\text{CH}_3\text{CO}\cdot\text{CH}_2\cdot\text{COOEt}$  (Geuther, 1863) is a light, colourless liquid having a faint, pleasant ethereal odour; it boils at  $181^{\circ}$  under ordinary pressure, and at  $74^{\circ}$  under 15 mm. pressure ( $181^{\circ}/760$  mm., and  $74^{\circ}/15$  mm.); the boiling-point at pressures below 30 mm. varies about  $1^{\circ}$  per mm.

*Acetoacetic acid*,  $\text{CH}_3\text{CO}\cdot\text{CH}_2\cdot\text{COOH}$ , is an unstable, very acid syrup, having a peculiar odour; it occurs naturally in diabetic urine, in which it can usually be recognized by

its odour, and the purple colour it forms with ferric chloride.

When heated, acetoacetic acid breaks up into acetone and carbon dioxide, and the same decomposition occurs when ethyl acetoacetate is boiled with dilute acids or alkalis. If, however, the ester be boiled with concentrated alcoholic potash, it is reconverted into acetic acid.

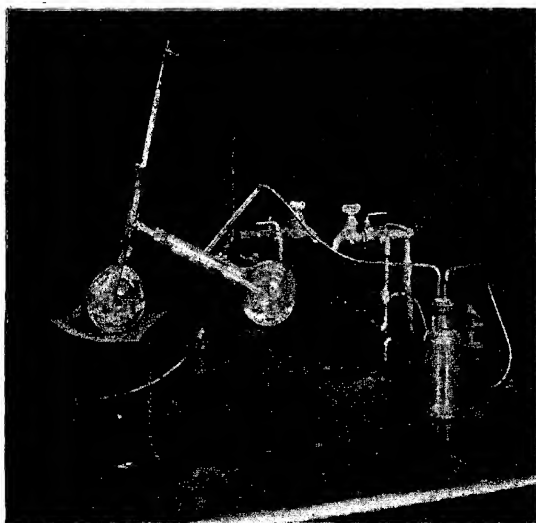
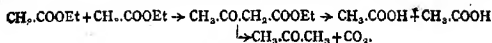


Fig. 20.—Distillation under Reduced Pressure.

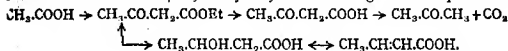
The molecular formula of ethyl acetoacetate deduced from the vapour-density is  $C_6H_{10}O_3$ . The hydrolysis to the monobasic acid,  $C_4H_6O_3$  ( $= C_3H_5O.COOH$ ), gives the rational formula  $C_3H_5O.COOEt$ . The further conversion of the ester and acid into acetone and carbon dioxide shows that the group  $C_3H_5O$  is acetonyl,  $CH_3.CO.CH_2$ , and at once leads to the constitutional formula  $CH_3.CO.CH_2.COOEt$  (Frankland, 1865).

This formula also accounts for the formation of the acetoacetate from ethyl acetate, and its reversion into acetic acid when hydrolysed with alcoholic potash.

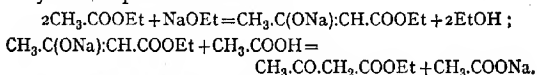


The presence of a ketonic group is confirmed by the conversion of the acetoacetate into a salt of the corresponding secondary-alcoholic acid when reduced with sodium amalgam. *β-Hydroxybutyric acid*,  $\text{CH}_3\text{CHOHCH}_2\text{COOH}$ , is a syrupy liquid resembling *β-lactic acid*; in its laevo-rotatory form it is often present in diabetic urine, in which it is the precursor of the accompanying acetoacetic acid and acetone.

Like *β-lactic acid* it is dehydrated to the corresponding ethylene derivative, namely *β-crotonic acid*,  $\text{CH}_3\text{CH}=\text{CHCOOH}$  (§ 132), when distilled with sulphuric acid, or even when boiled with strong caustic soda solution; in the latter case the action is reversible, so that the sodium crotonate and *β-hydroxybutyrate* exist together in equilibrium.



Ethyl acetoacetate is formed from ethyl acetate by a process of condensation (§ 146), with elimination of alcohol; the condensing agent is sodium ethoxide, as sodium has no action on ethyl acetate which has been carefully freed from alcohol. The mechanism of the process is somewhat complex, and probably involves the transient formation of various unstable intermediate additive compounds, which immediately break up in new directions.



**144. Ethyl Sodacetoacetate: Enolic and Ketonic Forms of Ethyl Acetoacetate**—*Ethyl sodacetoacetate*, the crystalline product of the action of sodium ethoxide on ethyl acetate, is also readily formed from ethyl acetoacetate. It was formerly believed that the sodium replaces one of the hydrogen atoms of the methylene group, yielding a derivative containing the atomic complex  $\text{CO.CHNa}$ ; but experimental evidence, too complicated to be considered here, leaves no doubt that ethyl sodacetoacetate is derived from the isomeric *ethyl β-hydroxycrotonate*,  $\text{CH}_3\text{C(OH):CHCOOEt}$ , an ester of an unsaturated alcoholic acid.

● Ethyl sodacetoacetate and ethyl *β-hydroxycrotonate* being derived from an alcoholic derivative of ethylene, are termed *enolic compounds*,\* as distinguished from ethyl acetoacetate, which when pure is a ketonic compound. Enolic compounds of this class are semi-acid in nature, and form metallic derivatives, the most characteristic of which are the ferric compounds, which are highly coloured.

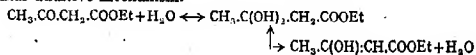
Ethyl acetoacetate itself becomes partially enolic under conditions favouring ionisation. A simple instance of this is given by the action of ferric chloride. When ionisation is prevented by dissolving the dry,

\* In the Geneva nomenclature (§ 102) the names of hydroxyethylenic derivatives contain the syllables *enol*; vinyl alcohol, for example, is *ethenol*, and *β-hydroxycrotonic acid*, *3-butenolic acid*.



alcohol-free ester in pure chloroform, no coloration at all is given by ferric chloride, whilst when it is dissolved in an ionising medium such as alcohol, it forms a purple-red with this agent, similar to that afforded by free acetoacetic acid under such conditions. If, however, the alcoholic solution be cooled to  $-90^{\circ}$  by solid carbon dioxide, so that the ions recombine, and the enolic form is reconverted into the ketonic form of the ester, the colour grows paler, and may quite disappear (Traube, 1896).

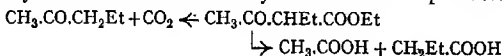
Whilst ethyl sodacetoacetate is homogeneous, ethyl acetoacetate under ordinary conditions is a mixture of two isomeric compounds; the true *ketonic ethyl acetoacetate*, and the isomeric *enolic ethyl  $\beta$ -hydroxycrotonate*. These compounds exist together in a state of dynamic equilibrium, the molecules of the one kind changing into those of the other, much as in the equilibrium between alcohol and acetic acid, and probably by a similar additive mechanism.



Compounds which behave according to two distinct constitutions, and are really balanced mixtures of two interconvertible and almost indistinguishable isomerides, are known as isodynamic or allelotropic compounds (*ἄλληλος* = reciprocally, *τροπή* = a turning round). Such compounds were formerly termed tautomeric or desmotropic compounds (*ταυτός* = same; *δεσμός* = a bond); the change was believed to be due to wandering hydrogen atoms.

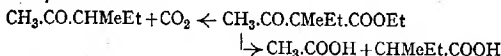
**145. The Acetoacetic Synthesis of Substituted Acetic Acids and Acetones.**—When ethyl sodacetoacetate, or the crude product of the action of sodium on ethyl acetate, is boiled with ethyl iodide, the pasty mass rapidly liquefies and becomes neutral, whilst sodium iodide separates. The liquid product is ethyl ethylacetoacetate, an ester of high boiling-point, which resembles ethyl acetoacetate, and is homologous with it.

On hydrolysis with concentrated alcoholic potash, this ester yields acetic and *ethyl-acetic* (normal butyric) *acid*, whilst with dilute aqueous acids or alkalies carbon dioxide and *ethyl-acetone* (methyl-*n*-propyl-ketone) are formed. If another alkyl iodide be substituted for the ethyl iodide, other alkylacetic acids and alkyl acetones are produced.



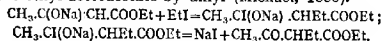
The new ester itself interacts with sodium ethoxide in the same way as acetoacetic ester, forming a similar crystalline sodium compound; and this is again neutralised by alkyl iodides, forming still more complex esters, with further separation of sodium iodide. These esters in turn undergo a similar hydrolysis, yielding dialkylacetic acids and dialkylacetones. When, for example, methyl iodide is

employed in succession to ethyl iodide, or *vice versa*, the initial product is ethyl methyl-ethyl-acetoacetate, from which on hydrolysis (acetic. and) methyl-ethyl-acetic ("active" valeric) acid, and methyl-ethyl-acetone (methyl-*sec*-butyl ketone) are obtained.

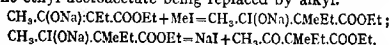


This somewhat complicated series of operations, known as the acetoacetic synthesis, was devised in the belief that the methyl hydrogen atoms of the ethyl acetate were successively replaced by sodium and exchanged for alkyl (Frankland, 1865). The formation of substituted acetones proved, however, that the mechanism is not so simple.

As we have seen, the complex esters which are alkyl-derivatives of acetoacetic ester, are formed directly from ethyl sodacetoacetate and its homologues. When ethyl iodide is added to ethyl sodacetoacetate, the negative iodine unites with the carbon atom to which the positive sodoxy-group is attached, and the ethyl radical combines with the adjacent carbon atom; but as the sodium at once separates with the iodine as sodium iodide, an ester of ethyl-acetoacetic acid remains. The practical result is the substitution of one of the methylene hydrogen atoms of the ethyl acetoacetate by alkyl (Michael, 1888).



The same result is obtained by the action of methyl iodide or other alkyl iodide on ethyl ethylsodacetoacetate, the second methylene hydrogen atom of the ethyl acetoacetate being replaced by alkyl.



But as the dialkylacetoacetic ester no longer contains methylene hydrogen which can be eliminated with hydroxyl as water, it is incapable of assuming an enolic form, and does not form a sodium derivative. The action cannot be carried further (compare § 232).

*Ethyl ethylacetoacetate*,  $\text{CH}_3\text{CO.CHEt.COOEt}$ , is a liquid which resembles ethyl acetoacetate, and can be isolated in a similar manner; it boils at 198°, and, as already stated, is resolved into acetic and butyric acids when heated with concentrated alcoholic potash. *Ethyl methylethylacetoacetate*,  $\text{CH}_3\text{CO.CMeEt.COOEt}$ , boils at 201°, and is similarly resolved into acetic and "active" valeric acids.

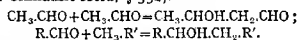
The alkyl-acetic acids thus synthesised are separable from the accompanying acetic acid either by fractional neutralisation, or by special methods, such as the precipitation of calcium butyrate by boiling its aqueous solution.



ethyl sodacetoacetate. By giving other values to these symbols the equations of other condensations are obtained, the great majority of which can be realised.

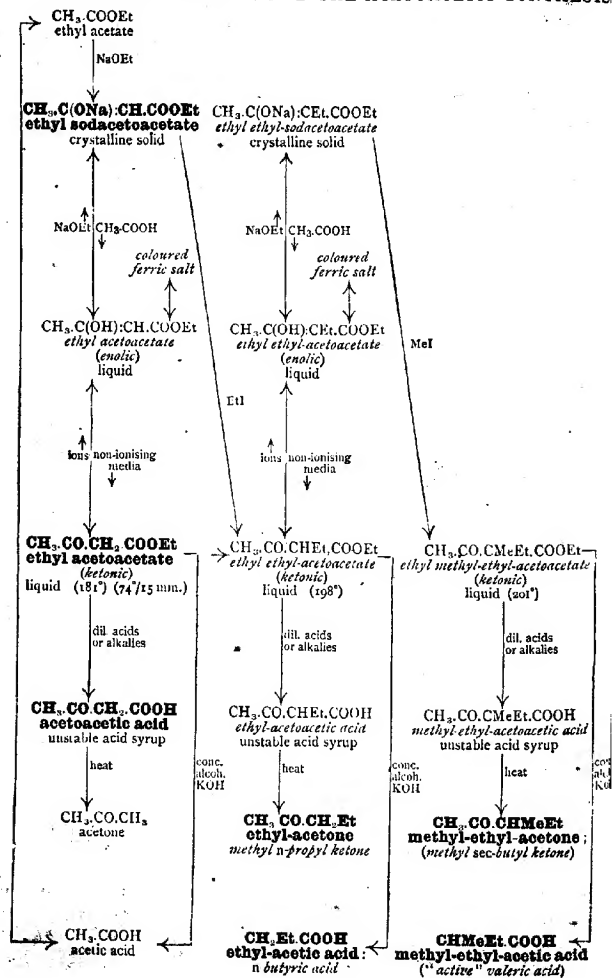
Ethyl oxalate condenses with ethyl acetate, forming *ethyl oxalacetate*,  $\text{COOEt.CO.CH}_2\text{COOEt}$  (§ 158), a compound which in many respects resembles ethyl acetoacetate. Ethyl acetate and acetone yield *acetylacetone*,  $\text{CH}_3\text{CO.CH}_2\text{CO.CH}_3$ , a liquid which boils at  $137^\circ$ , and like ethyl acetoacetate forms a sodium compound; the corresponding secondary alcohol, *aceto-sec-propyl alcohol*,  $\text{CH}_3\text{CO.CH}_2\text{CHOH.CH}_3$ , is obtained in a similar manner from acetaldehyde and acetone. Ethyl formate and acetone similarly yield the very unstable *acetoacetic aldehyde*,  $\text{CH}_3\text{CO.CH}_2\text{CHO}$ .

Acetaldehyde condenses with itself under the influence of alkali carbonates, forming  $\beta$ -hydroxybutyric aldehyde; the condensation is more conveniently effected by the action of dilute aqueous potassium cyanide on paraldehyde. *Aldol* or  $\beta$ -hydroxybutyric aldehyde,  $\text{CH}_3\text{CHOH.CH}_2\text{CHO}$  (Wurtz, 1872) is a syrupy liquid which boils at about  $70^\circ$  under 12 mm., but when heated under ordinary pressure decomposes at  $135^\circ$  into crotonaldehyde and water, thus behaving similarly to the acid. It gives the usual aldehyde reactions, and when warmed with silver oxide and water is oxidised to silver  $\beta$ -hydroxybutyrate, whence its constitution. There are many such condensations in which an aldehyde group unites with a methyl radical; they are termed generically aldol condensations (compare Cinnamic Acid, § 332).



**147. Synopsis.**—By the action of sodium on ethyl acetate in presence of alcohol, a ketonic ester, ethyl acetoacetate, is formed which can also exist in an enolic or hydroxy-ethylenic form, in which it yields metallic derivatives. Ethyl acetoacetate is directly convertible into acetic acid and acetone, and its alkyl substitution products, prepared synthetically from its sodium compound, are similarly resolvable into alkyl-acetic acids and alkyl-acetones.

## ETHYL ACETOACETATE AND THE ACETOACETIC SYNTHESIS



## CHAPTER XXVII

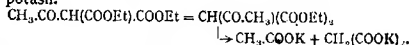
### THE SATURATED DIBASIC ACIDS

**148. Malonic Acid.\***—Malonic acid, the first homologue of oxalic acid, was originally obtained by oxidising malic acid (§ 158) with chromic acid mixture; it is more conveniently made from acetic acid by the cyanide synthesis.

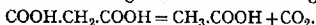
Warm chloroacetic acid solution is neutralised with potassium carbonate, and heated with the calculated amount of pure potassium cyanide until the vigorous action has quite subsided, and the cyanide has dissolved. The *potassium cyanacetate* thus formed is hydrolysed by boiling with concentrated hydrochloric acid, and the malonic acid is extracted with ether and crystallised (Kolbe, Müller, 1864).



Malonic acid may also be made by the acetoacetic synthesis. Ethyl sodacetate unites with *ethyl chloroformate*,  $\text{ClCOOEt}$  (§ 192), forming *ethyl acetomalonate*,  $\text{CH}_3\text{CO}\cdot\text{CH}(\text{COOEt})\text{COOEt}$ , a liquid which is converted into potassium acetate and potassium malonate when boiled with alcoholic potash.



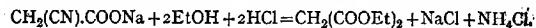
*Malonic acid*,  $\text{COOH}\cdot\text{CH}_2\cdot\text{COOH}$  (Dessaignes, 1858), forms long colourless crystals, and melts at  $132^\circ$ ; it is exceedingly soluble in water, and a fairly strong acid,  $K = 0.163$ . The constitution of the acid follows from its synthesis from acetic acid, and its direct resolution into carbon dioxide and the fatty acid, when heated a few degrees above its melting point.



Ethyl malonate, which is an important synthetic agent, is conveniently made from the alkali cyanacetate, a mixture of which with absolute alcohol is saturated with dry hydrogen chloride gas; or by passing hydrogen chloride gas into alcohol

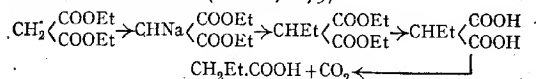
\* Malonic acid, as a three-carbon compound, ought properly to find its place in the preceding section, but it is more conveniently considered here.

in which crude calcium malonate is suspended. The cooled product is poured into ice-water, and the ethyl malonate extracted with ether, and fractionated in the usual manner.



*Ethyl malonate*,  $\text{CH}_2(\text{COOEt})_2$  (Conrad, 1880), is a heavy, colourless liquid, which has a pleasant aromatic odour, and boils at  $198^\circ$ . Like its lower homologue, ethyl oxalate, it is converted by ammonia into the corresponding crystalline amide, *malonamide*,  $\text{CH}_2(\text{CONH}_2)_2$ .

**148a. The Malonic Acid Synthesis.**—The utility of malonic acid in synthesis depends in the first place on its simple decomposition into acetic acid and carbon dioxide, and in the second place on the circumstance that the methylene hydrogen of its ester is replaceable by alkyl radicals. By alkylating ethyl malonate, and then setting the alkylmalonic acid free and decomposing it, any mono- or dialkyl-acetic acid is thus obtainable (Conrad, 1879).



On mixing ethyl malonate with sodium ethoxide in alcoholic solution, it is converted into *ethyl sodiomalonate*,  $\text{CHNa}(\text{COOEt})_2$  (or more probably,  $\text{COOEt}.\text{CH}:\text{C}(\text{ONa}).\text{OEt}$ ), a crystalline substance resembling ethyl sodacetoacetate; and on heating this substance with an alkyl iodide, such as ethyl iodide, in molecular proportion, an ethyl alkyl-malonate is obtained.

The ethyl iodide is poured into the crude sodium derivative, and the whole boiled on a water-bath until neutral, in the same way as in the acetoacetic synthesis, the ethereal salt being extracted with ether and fractionated.

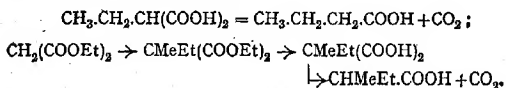
By repeating the treatment a second alkyl group can be introduced, just as with ethyl acetoacetate. *Ethyl ethyl-malonate*,  $\text{CHEt}(\text{COOEt})_2$ , is a liquid boiling at  $200^\circ$ ; *ethyl methyl-ethyl-malonate*,  $\text{CMeEt}(\text{COOEt})_2$ , boils at  $208^\circ$ .

To obtain the synthesised alkyl-acetic acid, the alkyl-malonic acid must be isolated. The alkyl-malonate is first converted into the sodium salt by boiling with strong caustic soda solution, and from this the sparingly soluble calcium salt is precipitated by concentrated calcium chloride. Enough oxalic acid is now added exactly to combine with the calcium, and the alkyl-malonic acid thus set free is extracted with ether, and recrystallised from water.



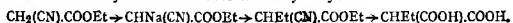
*Ethyl-malonic acid*,  $\text{CHEt}(\text{COOH})_2$ , is a crystalline substance, melting at  $111^\circ$ , which resembles malonic acid in every respect, and when heated at  $160^\circ$  is resolved into carbon dioxide and ethyl-acetic acid; the ethyl-acetic acid thus prepared boils at  $163^\circ$ , and is identical with normal butyric acid, a further synthesis of which is afforded.

*Methyl-ethyl-malonic acid*,  $\text{CMeEt}(\text{COOH})_2$ , melts at  $118^\circ$ , and when heated is similarly resolved into carbon dioxide and "active" valeric acid.



The malonic synthesis of substituted acetic acids is in some respects preferable to the acetoacetic synthesis, as the yields are better; and the resulting acids do not need purification; on the other hand, ethyl malonate is more difficult to make than ethyl acetoacetate and therefore more expensive.

*Ethyl cyanacetate*,  $\text{CH}_2(\text{CN})\cdot\text{COOEt}$ , a liquid boiling at  $207^\circ$ , may be substituted for the malonate, as its methylene hydrogen is similarly replaceable by sodium and alkyl; it is made by boiling ethyl chloracetate with potassium cyanide. The alkylated cyanacetates yield the same products as the alkylated malonates when hydrolysed.



**149. Succinic Acid.**—Oxalic and malonic acids are the lowest members of a homologous series of acids, the succinic or oxalic series, the next member of which is succinic acid.

Succinic acid was originally obtained by distilling amber (*succinum*), and is also formed in the alcoholic fermentation of sugar, and by oxidation of many fats and fatty acids with nitric acid; it is most conveniently prepared by fermenting tartaric or malic acid.

*Succinic acid*,  $\text{COOH}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{COOH}$  (Agricola, 1550), is a colourless, crystalline substance, which melts at about  $185^\circ$  and boils at  $235^\circ$ , at the same time partially decomposing; it burns with a blue non-luminous flame. It has an unpleasant acid taste, but is a much weaker acid than either of its lower homologues, its dissociation constant being  $K=0.0067$ .

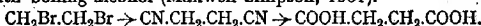
When heated with hydriodic acid and phosphorus, succinic acid is reduced to *n*-butane, of which it is therefore a derivative; as it is a dibasic acid, its molecule must contain two carboxyl groups. The only formula complying with these



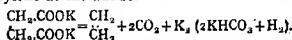
conditions is that which is given above; it is confirmed by direct synthesis of the acid from ethylene bromide.

On boiling ethylene bromide with alcohol and pure potassium cyanide, *ethylene cyanide* or *succinonitrile*,  $\text{CN} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CN}$ , a colourless crystalline substance melting at  $54^\circ$ , is obtained, portions of which can be seen in the reflux condenser towards the end of the operation. After filtering off potassium bromide, water and caustic soda are added, and the boiling is continued as long as ammonia is evolved.

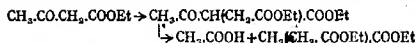
The product, which now contains sodium succinate, is acidified with dilute sulphuric acid and evaporated to dryness, and the succinic acid is extracted from the residue with boiling alcohol (Maxwell Simpson, 1861).



Conversely, succinic acid is converted into ethylene by simply electrolyzing a strong solution of its potassium salt; hydrogen is set free at the kathode, and ethylene at the anode.



Succinic acid can also be synthesised from ethyl acetoacetate or ethyl malonate by boiling the respective sodium compounds with ethyl chloroacetate. The *ethyl acetosuccinate*,  $\text{CH}_3 \cdot \text{CO} \cdot \text{CH}(\text{CH}_2 \cdot \text{COOEt}) \cdot \text{COOEt}$ , which is formed in the first case, is subjected to the "acid" hydrolysis by boiling with concentrated alcoholic potash, and yields acetic and succinic acids.



**150. Derivatives of Succinic Acid.**—Succinic acid is a dibasic acid, and its derivatives are analogous to those of oxalic acid. The *alkali succinates*, however, are very soluble; even *calcium succinate* is soluble in water, and can only be precipitated in presence of alcoholic ammonia. The *basic ferric salt*, formed by adding ferric chloride to a neutral solution of a succinate, is a brown gelatinous precipitate.

On the other hand, the ester, *ethyl succinate*,  $\text{C}_2\text{H}_4(\text{COOEt})_2$ , is an oily liquid which boils at  $216^\circ$ , and closely resembles the corresponding oxalate; it is formed by warming the acid and alcohol with a little concentrated sulphuric acid, and isolated by pouring into water.

Like the oxalate, ethyl succinate is converted by aqueous ammonia into the corresponding diamide, *succinamide*,  $\text{C}_2\text{H}_4(\text{CONH}_2)_2$ , an insoluble crystalline powder; on heating ammonium succinate, however, or succinamide itself, ammonia is given off and a product of a new type formed, termed *succinimide*.

*Succinimide*,  $\begin{array}{c} \text{CH}_3 \cdot \text{CO} \\ \text{CH}_2 \cdot \text{CO} \end{array} \text{NH}$  (Fehling, 1844), a crystalline substance melt-

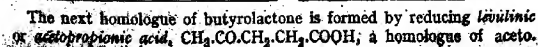
When succinic acid is distilled, either alone, or with phosphorus oxychloride, it loses water (not carbon dioxide, like malonic acid), and forms an anhydride. *Succinic anhy-*

*Succinyl chloride*,  $\text{COClCH}_2\text{CH}_2\text{COCl}$ , formed by the action of phosphorus pentachloride on ethyl succinate, is a liquid which resembles oxalyl chloride, and is hydrolysed by water in the normal manner to succinic and hydrochloric acids.

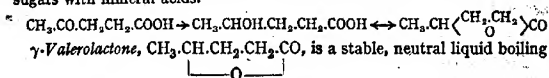
**151. The Lactones.**—When succinyl chloride or succinic anhydride is reduced with sodium amalgam, it is converted, not into the aldehyde, as was originally supposed, but into an isomeride derived from butyric acid, termed butyrolactone (Fittig, 1880); the same compound is produced by reducing *aldheydropropionic acid* (succinic semi-aldehyde),  $\text{CHO} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{COOH}$ , with sodium amalgam.

liquid boiling at 206°, which is formed both by reducing succinyl chloride, and by distilling  $\gamma$ -chlorobutyric acid.

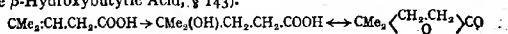
Butyrolactone is converted into succinic acid by oxidation with chromic acid, but when warmed with caustic baryta solution is hydrolysed to the barium salt of  $\gamma$ -hydroxybutyric acid; it is thus an internal ethereal salt of  $\gamma$ -hydroxybutyric acid, in which the carboxyl has entered into combination with the alcoholic hydroxyl.



acetic acid which contains the ketonic group in the  $\gamma$ -position; levulinic acid may be made synthetically, but is best prepared by the hydrolysis of sugars with mineral acids.



at  $207^\circ$ ; it is converted by caustic alkalis into a salt of  $\gamma$ -hydroxyvaleric acid, and is reduced to valeric acid itself by sodium amalgam in acid solution. *Isocapro lactone*,  $\text{CMe}_2 \left( \begin{array}{c} \text{CH}_2\text{CH}_3 \\ \text{O} \end{array} \right) \text{CO}$  (Fittig, 1880), the first member of this class to be recognised, is obtained as a neutral oil by warming an unsaturated acid, pyroterebic acid, with dilute sulphuric acid (compare  $\beta$ -Hydroxybutyric Acid, § 143).

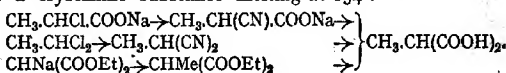


It is only hydroxyl-groups in the  $\gamma$ - and more remote positions which interact in this manner to form lactones;  $\alpha$ - and  $\beta$ -hydroxy-acids scarcely ever form such compounds, the stereometric conditions (§ 288) being unfavourable. Hydracrylic acid is converted into the unsaturated acrylic acid by dehydration, and although lactic and glycollic acids form internal esters or lactides, two molecules of the acid enter into the action.

The  $\gamma$ -hydroxyacids cannot be isolated, but they exist in solution in equilibrium with the lactones, with which they are interconvertible. Their esters, etc., are known.

**152. The Succinic Series of Acids.**—Succinic acid is derived from normal butane and ethylene, and there is an isomeric isosuccinic acid similarly related to isobutane and ethylidene; this acid is formed from both  $\alpha$ -chloropropionic acid and ethylidene chloride by the cyanide synthesis, and from malonic acid by the malonic synthesis.

*Isosuccinic* or *ethylidenesuccinic acid*,  $\text{CH}_3\cdot\text{CH}(\text{COOH})_2$ , is a crystalline substance melting at  $134^\circ$ .



As a substituted malonic acid, isosuccinic acid is resolved by heat, not into water and an anhydride, but into carbon dioxide and the related monocarboxylic acid, propionic acid.

It is a general rule that when the carboxyl groups of dicarboxylic acids are attached to adjacent carbon atoms, the acids are resolved into anhydrides by heat, but that when the groups are attached to the same carbon atom, monocarboxylic

acids and carbon dioxide are formed; succinic acid is the type of the first class of compounds, and malonic acid of the second.



The isomerism of the higher members of the succinic series is naturally very complex. In the first place, in addition to the alkyl derivatives of malonic acid, which have already been considered, there are similar derivatives of succinic acid. *Pyrotartaric* or *methylsuccinic acid*,  $\text{COOH}\cdot\text{CHMe}\cdot\text{CH}_2\cdot\text{COOH}$ , is formed, together with *pyroracemic acid*, by distilling tartaric acid, and can also be made from propylene bromide by the cyanide synthesis.

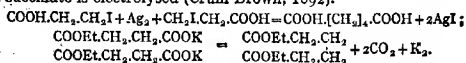
The symmetrical dialkylsuccinic acids, namely, those in which the methylene hydrogen is only partially substituted, are capable of existing in stereoisomeric forms, corresponding with the stereoisomeric dibromo- and inactive dihydroxysuccinic acids (§ 163), the methylene carbon atoms becoming asymmetrical.

*Para-dimethylsuccinic acid* is sparingly soluble in water, and melts at  $194^\circ$ ; the isomeric *anti-dimethylsuccinic acid* is more freely soluble, and melts at  $123^\circ$ .

In addition to the substituted succinic acids, there are a number of acids in which the carboxyl groups are attached to carbon atoms which are not adjacent. The most prominent of these is adipic acid, an acid which is closely related to the sugars.

*Adipic acid*,  $\text{COOH}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{COOH}$  (Laurent, 1839), is a crystalline substance, melting at  $149^\circ$ . It is best prepared by oxidising hexanaphthene,  $\text{C}_8\text{H}_{12}$  (§ 287) with nitric acid.

Adipic acid can be synthesised by heating  $\beta$ -iodopropionic acid with reduced silver; its ethyl salt is also formed synthetically when ethyl potassium succinate is electrolysed (Crum Brown, 1892).



The principal members of the oxalic-succinic series are tabulated below; the higher members are formed by the oxidation of fats, cork, etc., with nitric acid.

Acid.	Constitution.	M.p.	K.
Oxalic .	$\begin{array}{c} \text{COOH} \\ \text{COOH} \end{array}$	—	10
Malonic .	$\text{CH}_2 \begin{array}{c} \text{COOH} \\ \text{COOH} \end{array}$	132°	0·163
Succinic .	$\begin{array}{c} \text{CH}_2\text{COOH} \\ \text{CH}_2\text{COOH} \end{array}$	185°	0·0065
Glutaric .	$\text{CH}_2 \begin{array}{c} \text{CH}_2\text{COOH} \\ \text{CH}_2\text{COOH} \end{array}$	97°	0·0048
Adipic .	$\begin{array}{c} \text{CH}_2\text{CH}_2\text{COOH} \\ \text{CH}_2\text{CH}_2\text{COOH} \end{array}$	149°	0·0037
Pimelic .	$\text{CH}_2 \begin{array}{c} \text{CH}_2\text{CH}_2\text{COOH} \\ \text{CH}_2\text{CH}_2\text{COOH} \end{array}$	105°	0·0036
Suberic .	$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CH}_2\text{COOH} \\ \text{CH}_2\text{CH}_2\text{CH}_2\text{COOH} \end{array}$	140°	0·0031
Azelaic .	$\text{CH}_2 \begin{array}{c} \text{CH}_2\text{CH}_2\text{CH}_2\text{COOH} \\ \text{CH}_2\text{CH}_2\text{CH}_2\text{COOH} \end{array}$	106°	0·0030
Sebacic .	$\begin{array}{c} \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH} \\ \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH} \end{array}$	133°	0·0023

There are several noteworthy features about this series. The melting-points vary irregularly, the acids having an odd number of carbon atoms in the molecule melting at relatively lower temperatures than those having an even number. The odd acids commencing with malonic acid are also exceedingly soluble, whereas the even acids are only sparingly so.

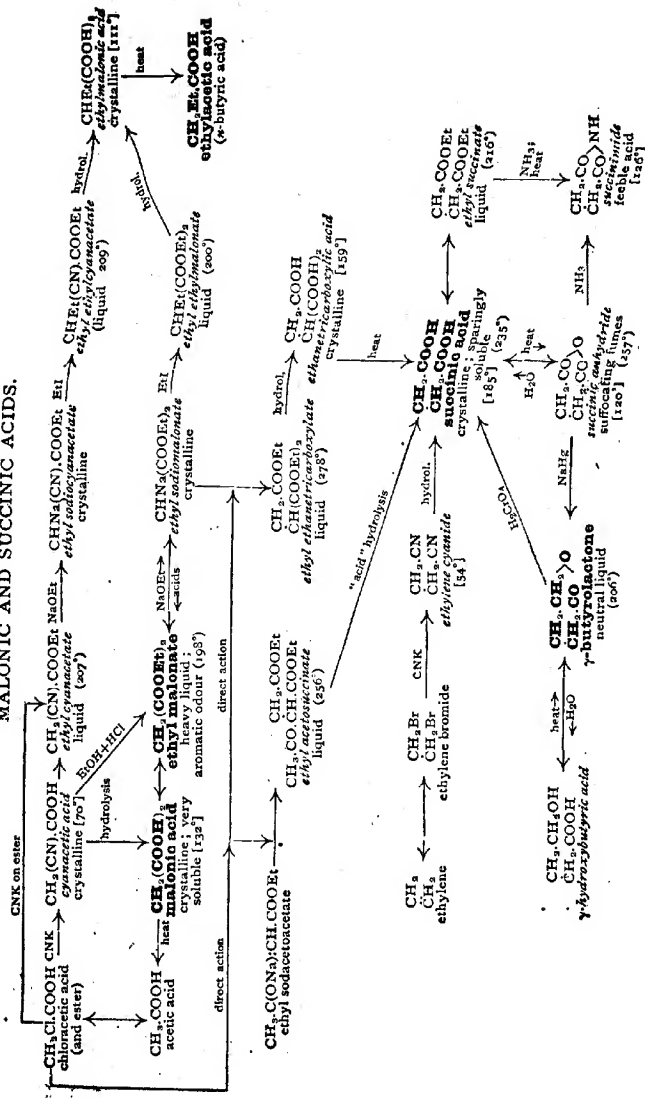
The rapid diminution in the acidity is also very striking, and shows the importance of the relative positions of the negative or acidifying groups. Oxalic acid, in which the carboxyl groups are adjacent, is a powerful acid, whereas sebacic acid, in which the carboxyl groups, although identical with those of oxalic acid, are separated by a chain of eight methylene groups, is little stronger than the monobasic fatty acids.

A further feature of interest is the mechanism of the formation of anhy-

drides. Oxalic and malonic anhydrides appear to be incapable of existence; the former acid yields carbon monoxide and dioxide under conditions which might otherwise determine the formation of an anhydride, whilst malonic acid and its derivatives yield carbon dioxide and acetic acids. Succinic acid and its alkyl-substitution products form anhydrides with ease, and glutaric acid and its derivatives also form anhydrides, although not so readily. Adipic acid and its higher homologues do not form anhydrides, and the obvious explanation of this fact, bearing in mind the stereometrical ideas developed in connection with lactic acid, is that the carboxyl-groups in these acids are too far apart to interact (see also § 288). That they do not influence one another materially is shown by the smallness of the dissociation constants of the acids.

**158. Synopsis.**—Malonic and succinic acids are methylene-dicarboxylic and ethylene-dicarboxylic acid respectively, and belong to the oxalic series of acids. The members of this series are divided into three classes—derivatives of malonic acid, derivatives of succinic acid, and acids in which the two carboxyl groups are united to non-adjacent carbon atoms.

## MALONIC AND SUCCINIC ACIDS.



## CHAPTER XXVIII

### THE UNSATURATED DIBASIC ACIDS

**154. Maleic and Fumaric Acids.**—Corresponding with the succinic series of acids, there are a number of dibasic acids which are similarly related to the higher olefines and acetylenes. The chief of these olefinic acids are maleic and fumaric acids.

When malic or hydroxy-succinic acid (§ 158) is distilled, it loses water, in the same way as hydracrylic acid; but instead of a single unsaturated acid, two isomeric compounds are produced. Maleic acid and its anhydride pass over, whilst fumaric acid remains behind; by heating the malic acid cautiously at 130–140°, fumaric acid is formed alone.

*Maleic acid*,  $\begin{matrix} \text{H.C.COOH} \\ | \\ \text{H.C.COOH} \end{matrix}$  (Lassaigne, 1819), is a crystalline

substance of disagreeable acid taste; it melts at 130°, and boils at 160°, at the same time partially decomposing into water and its anhydride; it is very soluble, even in cold water, and is a strong acid,  $K=1.17$  (compare Acrylic acid,

§ 132). *Maleic anhydride*,  $\begin{matrix} \text{H.C.CO} \\ | \quad \diagup \text{O} \\ \text{H.C.CO} \end{matrix}$ , is a crystalline substance, which melts at 60°, and is readily rehydrated to the acid.

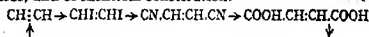
*Fumaric acid*,  $\begin{matrix} \text{H.C.COOH} \\ | \quad | \\ \text{COOH.C.H} \end{matrix}$  (Lassaigne, 1819), which

occurs naturally in the common fumitory (*fumaria*), is a crystalline substance of agreeable acid taste, and is practically insoluble in cold water; it is a much weaker acid than its isomeride,  $K=0.093$ . Fumaric acid melts only with difficulty, but sublimes to some extent at about 200°, at the same time being partially converted into maleic anhydride and water; the decomposition becomes quantitative when the acid is

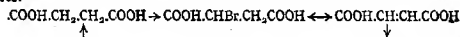


heated with dehydrating agents. Conversely, when maleic acid is heated at  $130^{\circ}$ , or with water at  $200^{\circ}$ , it is gradually converted into fumaric acid.

Maleic and fumaric acids are dibasic acids, and both yield acetylene when the aqueous solutions of their alkali salts are electrolysed. Fumaric acid can also be made by the cyanide synthesis from *acetylene diiodide*,  $\text{CHI}:\text{CHI}$ , a crystalline substance which is made by passing acetylene into an alcoholic solution of iodine. Both acids are therefore ethylene-dicarboxylic acids, and of identical constitution.

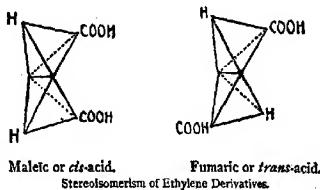


This conclusion is confirmed by their relation to succinic acid; they are reduced to this acid by sodium amalgam or hydriodic acid, and fumaric acid is formed by simply boiling monobromosuccinic acid (§ 158) with water.



Further, both acids, as ethylene derivatives, combine with hydrogen bromide, forming bromosuccinic acid, and with bromine, forming the dibromosuccinic acids.

**155. Stereoisomerism of Ethylene Derivatives.**—The undoubted structural identity of maleic and fumaric acids necessitates a further development of the conception of stereoisomerism.

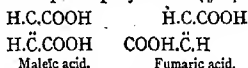


If carbon atoms be represented as regular tetrahedra, the nuclear tetrahedra in ethylene derivatives must be linked edge to edge; formulæ thus become possible for these acids, which are structurally identical but stereometrically different, and by the absence of symmetry in their relation to one another symbolise the great physical difference between the two isomerides (compare Stereoisomeric Lactic Acids, § 140).

The pairs of groups which are on the same (*cis*) side of the tetrahedra in the one formula are on opposite (*trans*) sides in the other (Van't Hoff, 1887); it is noteworthy that the *cis*-formula can be divided symmetrically by a plane passing through the points of attachment of the groups, whilst the

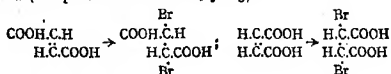
*trans*-formula can only be so divided through the axis along which the two nucleal carbon tetrahedra are linked.

As in the case of the optically active compounds, it is more convenient to use the plane projections (§ 141) of the formulæ.

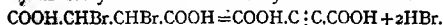


There is little difficulty in assigning the formulæ to the respective modifications. The compound in the molecule of which the carboxyl groups are nearest will obviously form an anhydride the more readily; the unstable or labile maleic acid is therefore the *cis*-modification, and is represented by the plane-symmetrical formula, whilst the stable fumaric acid is the *trans*-modification and is represented by the axial-symmetrical formula. Maleic acid is therefore *cis*-ethylene-dicarboxylic acid, and fumaric acid, *trans*-ethylene-dicarboxylic acid. Many such pairs of isomerides are known, the labile or *cis*-modifications, being invariably more soluble than the stable or *trans*-modifications, and also stronger acids, owing to the greater proximity of the carboxyl groups (§§ 152, 288).

The above conclusions as to the stereoisomerism of maleic and fumaric acids, and of maleoid and fumaroid compounds in general, are confirmed by their behaviour with bromine, of which, as ethylene derivatives, they take up a molecular proportion. Whilst fumaric acid yields ordinary dibromosuccinic acid, identical with that obtained by directly brominating succinic acid, maleic acid yields the stereoisomeric *isodibromosuccinic acid* (compare Tartaric Acids, § 163).\*



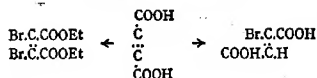
**156. Acetylene-dicarboxylic Acid.**—The acetylene derivative corresponding with maleic and fumaric acids is formed by boiling dibromosuccinic acid with alcoholic potash, in the same way as acetylene itself from ethylene dibromide.



*Acetylene-dicarboxylic acid*,  $\text{COOH.C} : \text{C.COOH}$  (Bandrowsky, 1879), is a crystalline substance, melting at  $179^\circ$ ; it is an exceedingly powerful acid, of the same order as the mineral acids; the dissociation constant being too large to be measured.

Acetylene-dicarboxylic acid is convertible into derivatives both of maleic and fumaric acids; the ethyl salt unites with bromine, forming ethyl dibromo-maleate, whilst the acid itself unites with hydrogen bromide, forming bromo-fumaric acid.

\* The student is strongly urged to study these space-actions with the aid of the cardboard tetrahedra mentioned under Lactic Acid; half-a-dozen of these can be made in a few minutes, and will save many hours.



*Potassium hydrogen acetylene-dicarboxylate*,  $\text{COOH.C}\equiv\text{C.COOK}$ , is a sparingly soluble substance, which is resolved into carbon dioxide and potassium propiolate (§ 134) when boiled with water.

More complex acid acetylene derivatives have also been prepared, of progressively decreasing stability.

**157. Synopsis.**—Maleïc and fumaric acids are the ethylene derivatives corresponding with succinic acid. They are structurally identical, but their spacial configurations are different, the labile maleïc acid having the *cis*- or plane-symmetrical formula, and the stable fumaric acid the *trans*- or axial-symmetrical formula. Acetylene-dicarboxylic acid is the corresponding acetylene derivative.



## CHAPTER XXIX

### THE VEGETABLE ACIDS

**158. The Malic Acids: Oxalacetic Acid.**—The sourness of unripe fruit is almost always due to tartaric, citric, or malic acids, which together with oxalic acid and a few others, may be termed the vegetable acids. Malic and tartaric acids are hydroxy-derivatives of succinic acid. Sour apples contain a considerable quantity of malic acid, which, however, is more economically obtained from rhubarb, or unripe mountain ash berries.

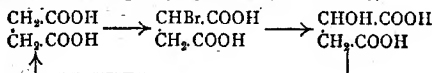
The juice expressed from the stalks or berries is concentrated, and the acid neutralised with boiling milk of lime. The normal calcium malate thus precipitated is dissolved in hot dilute nitric acid, and recrystallised as the acid salt, which forms much better defined crystals. The free acid is prepared by decomposing the lead salt with hydrogen sulphide.

*l-Malic acid*,  $\text{COOH} \cdot \text{CHOH} \cdot \text{CH}_2 \cdot \text{COOH}$  (Scheele, 1785), is a deliquescent, semi-crystalline substance, which forms soft, warty masses, melting at  $100^\circ$ . It is a dibasic acid, as it forms two classes of salts, such as the calcium salts mentioned above; the dissociation constant is  $K = 0.0395$ . *Lead malate*, precipitated by lead acetate from a neutral solution of an alkali malate, is characteristic, as it is insoluble in ammonia, and melts to a sticky paste when boiled with water.

Malic acid is an alcohol, for, by the action of acetyl chloride, *ethyl malate* is converted into *ethyl acetyl-malate*,  $\text{COOEt} \cdot \text{CH}(\text{OAc}) \cdot \text{CH}_2 \cdot \text{COOEt}$ . Its constitution as hydroxy-succinic acid is fully proved by analysis and synthesis; it is reduced to succinic acid when heated with hydriodic acid, and its inactive modification (see below) is formed when bromosuccinic acid is treated with silver oxide and water.

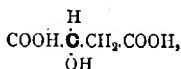
*Bromosuccinic acid*, a crystalline substance melting at  $159^\circ$ , is made by heating succinic acid, or crude succinic anhydride, in a reflux apparatus

with bromine and red phosphorus; the *bromo-succinyl bromide* thus formed is hydrolysed by shaking with hot water for a short time, and the resulting *bromo-succinic acid* is quickly crystallized (Volhard, 1887).



Like oxalic acid, malic acid forms two amides, namely, *malamide*  $\text{C}_2\text{H}_3(\text{OH})(\text{CONH}_2)_2$ , and *malamic acid*,  $\text{CONH}_2\text{C}_2\text{H}_3(\text{OH}).\text{COOH}$ ; they are both crystalline substances.

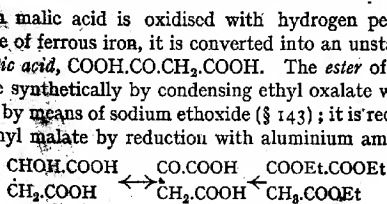
The malic acid molecule contains an asymmetrical carbon atom—



and the acid, therefore, like lactic acid, assumes three stereoisomeric forms, in two of which it is optically active; with the exception of differences in the solubilities of their salts, the three acids are chemically identical.

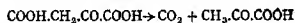
*Natural malic acid*,  $\text{H.C.OH}$ , is levogyrate,  $[\alpha]_D = -3.3^\circ$ . The antipodal *dextromalic acid*,  $\text{OH.C.H}$ ,  $[\alpha]_D = +3.3^\circ$ , is formed by the partial reduction of tartaric acid, and by the action of nitrous acid on aspartic acid (§ 221). *Inactive malic acid*,  $\begin{array}{c} \text{COOH} \\ \text{CH}_2\text{COOH} \\ \text{COOH} \end{array}$ , formed by mixing the solutions of equal weights of the active acids, is formed, not only synthetically, but also by the partial reduction of racemic acid; like inactive lactic acid, it can be resolved into its components by fractional crystallisation with alkaloids, the cinchonine salt being the most suitable.

When malic acid is oxidised with hydrogen peroxide in presence of ferrous iron, it is converted into an unstable acid, *oxalacetic acid*,  $\text{COOH.CO.CH}_2\text{COOH}$ . The ester of this acid is made synthetically by condensing ethyl oxalate with ethyl acetate by means of sodium ethoxide (§ 143); it is reconverted into ethyl malate by reduction with aluminium amalgam.



Oxalacetic acid readily loses carbon dioxide, forming pyruvic acid; as a ketone it forms a *hydrasone*, which is similarly converted into pyruvic acid.

cemic hydrazone when heated with water, but into a more complex acid derived from pyrazolone (§ 409) in presence of hydrogen ions, of the concentration of which it therefore affords a measure.

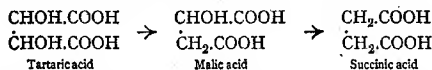


**159. Tartaric Acid.**—The chief source of ordinary tartaric acid is *argol*, or impure potassium hydrogen tartrate, which is a constituent of grape juice, and, being insoluble in alcohol, separates as a crystalline "crust" in the preparation of wine; the brownish argol may be decolorised by digesting its hot solution with animal charcoal, and after recrystallisation from hot water, is known as *cream of tartar*.

When cream of tartar is boiled with water and chalk, it is converted, half into insoluble calcium tartrate, and half into soluble potassium tartrate; on mixing the filtered solution of the latter with calcium chloride solution, the second moiety of the acid is precipitated; finally the washed calcium tartrate is decomposed with the calculated amount of dilute sulphuric acid, the tartaric acid being evaporated, and recrystallised until pure.

*Tartaric acid*,  $\text{COOH} \cdot \text{CHOH} \cdot \text{CHOH} \cdot \text{COOH}$  (Scheele, 1769), crystallises in large, colourless prisms of pure and agreeable acid taste; its dissociation constant is  $K = 0.097$ . It melts at  $170^\circ$ , but chars at a slightly higher temperature, giving off fumes resembling those of burnt sugar, and yielding, amongst other products, pyroracemic and pyrotartaric acids.

That tartaric acid is dihydroxysuccinic acid is proved by its successive reduction to malic and succinic acids, when heated with hydriodic acid, and by various syntheses (§ 161).



Tartaric acid is a dibasic acid; it not only forms well-defined acid salts, such as *potassium hydrogen tartrate*,  $\text{KHC}_4\text{H}_4\text{O}_6$ , but also stable dialkyl esters, such as the liquid *ethyl tartrate*,  $\text{Et}_2\text{C}_4\text{H}_4\text{O}_6$ , and the crystalline *methyl tartrate*, both of which can be distilled unchanged under low pressure. The molecule contains two alkylic hydroxyl groups, for ethyl tartrate is converted by acetyl chloride into crystalline *ethyl diacetotartrate*, melting at  $67^\circ$ .

The tartrates are substances of great antiquity. Cream of tartar was known to the ancient Greeks, and *tartar emetic*,  $\text{K}(\text{SbO})\text{C}_4\text{H}_4\text{O}_6 + \frac{1}{2}\text{H}_2\text{O}$ , a basic, but soluble antimony salt, made by boiling cream of tartar with antimonious oxide and water, was used in the middle ages. *Sodium potassium tartrate*, or *Rochelle salt*,  $\text{KNaC}_4\text{H}_4\text{O}_6 + 4\text{H}_2\text{O}$  (Seignette, 1672), is

a well-defined crystalline substance, formed by dissolving cream of tartar in sodium carbonate solution. *Calcium tartrate*, which is thrown down when calcium chloride is well stirred with a neutral solution of a tartrate, is soluble in acetic acid and in caustic soda, and thus easily distinguished from calcium oxalate; it is reprecipitated on warming the alkaline solution.

The tartrates are further distinguished by two other properties. They are readily oxidisable (§ 160), and thus reduce silver solutions; and like other poly-hydroxy-compounds, they prevent the precipitation of copper and iron by alkalies.

On warming a neutral solution of a tartrate with ammoniacal silver nitrate, a silver mirror is deposited on the sides of the vessel, the acid being oxidised to carbonic and oxalic acids; and on adding caustic soda to a solution of copper sulphate containing Rochelle salt, a deep blue alkaline solution is obtained (Fehling, 1849), which is used for the detection and estimation of substances, such as sugars, which reduce copper only in alkaline solution.

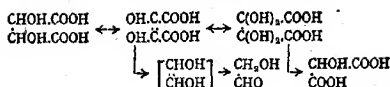
**160. Dihydroxymaleic and Dihydroxytartaric Acids.**—When hydrogen peroxide is added to a solution of a tartrate, to which a little ferrous salt has been added, the solution turns yellow, and on adding caustic alkali an intense violet colour is developed. The same result is obtained on exposing the ferrous solution to air in direct sunlight.

This reaction, which affords a delicate test for tartrates, is due to the formation of an oxidation product, dihydroxymaleic acid, which may be precipitated from the yellow solution at a low temperature by adding fuming sulphuric acid.

*Dihydroxymaleic acid*,  $\begin{matrix} \text{OH.C.COOH} \\ \text{OH.C.COOH} \end{matrix}$  (Fenton, 1894), is a sparingly soluble crystalline substance, and a strong acid,  $K=7.2$ . When warmed with water it effervesces, decomposing into carbon dioxide and glycollic aldehyde, and is hence an energetic reducing agent. It is reduced to racemic and succinic acids by hydriodic acid at  $100^{\circ}$ , and is oxidised by bromine to dihydroxytartaric acid.

*Dihydroxytartaric acid*,  $\begin{matrix} \text{C(OH)}_2\text{COOH} \\ \text{C(OH)}_2\text{COOH} \end{matrix}$  is a crystalline solid, which is more soluble and less acid than the maleic derivative;  $K=1.24$ . Its sodium salt is practically insoluble, and therefore serves as a test for sodium. Dihydroxytartaric acid is also formed by the action of nitric acid on protocatechuic acid (§ 310); it is reconverted into the maleic derivative when reduced with zinc and sulphuric acid, and when heated with water is resolved into carbon dioxide and tartronic acid (§ 129).





**161. Racemic and Meso-Tartaric Acids.**—Ordinary tartaric acid is optically active and dextrogyrate,  $[\alpha]_D = +14^\circ$ , as its formula contains asymmetrical carbon. But as there are two asymmetrical atoms, there are four stereoisomeric acids, namely, dextro- and levo-tartaric acids, and racemic and mesotartaric acids; the two last are optically inactive.

Racemic acid, the inactive acid corresponding with inactive malic and lactic acids, is formed when tartaric acid is heated with water (1 mol.) at  $175^\circ$ ; it was first obtained from the mother-liquor of this compound, in which it is doubtless produced during the evaporation.

Racemic acid is more conveniently made by boiling tartaric acid with excess of concentrated caustic soda; sodium mesotartarate is first formed, but is slowly converted into sodium racemate by further isomeric change; the acid is then isolated by means of its insoluble calcium salt, in the same way as tartaric acid. The racemic acid crystals are readily picked out from any crystals of unchanged tartaric acid, as they are efflorescent.

Many optically active compounds are similarly converted into inactive modifications when heated alone or with reagents, and such optical inversions are known generically as racemisations; part of the optically active molecules are transformed into their antipodes, which unite with the remainder, forming the racemic compound.

*Racemic acid*,  $\begin{array}{c} \text{CHOH.COOH} \\ \text{CHOH.COOH} \end{array} + \text{H}_2\text{O}$  (Kestner, 1822), crystallises with water, which it slowly loses even at the ordinary temperature; the anhydrous acid melts at  $206^\circ$ .

Racemic and tartaric acids were the first isomeric compounds recognised, (Berzelius, 1829). The metallic racemates differ from the tartrates much in the same way as the inactive from the active lactates; *calcium racemate* is insoluble in acetic acid. The chemical relations of the acid, however, are practically identical with those of tartaric acid, and its constitution is therefore the same.

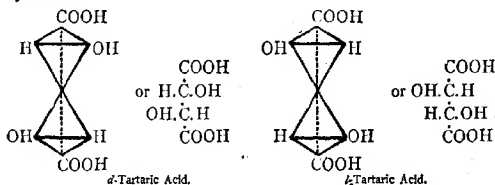
Racemic acid and the second inactive acid, mesotartaric acid, are the products obtained in all syntheses of the tartaric acids (compare Synthesis of Lactic Acid, § 137). Calcium racemate is formed when calcium dibromo-



In any case separation only occurs when the crystals are deposited below  $28^{\circ}$ , which is the transition temperature, at which the racemate exists in equilibrium with its optically active constituents. Above this temperature the active constituents reunite to form the racemate. The crystals are hemihedral, those of the dextrogyrate acid being dextrohemihedral, and those of the levogyrate acid, levohemihedral. It was this essentially asymmetrical structure of the crystals, which first led to the suggestion that the molecules are asymmetrical (Pasteur), and eventually to the theory of stereoisomerism.

*Lævotartaric acid* (Pasteur, 1851) resembles ordinary tartaric acid in every respect, with the exception that it is levogyrate ( $[\alpha]_D = -14^{\circ}$ ), and that its crystals are mirror images of those of the dextro-acid. On mixing its concentrated solution with one of ordinary tartaric acid, much heat is evolved, and racemic acid crystallizes out (Pasteur).

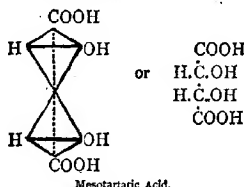
**163. The Isomerism of the Tartaric Acids.**—The isomerism of racemic acid and its constituents is analogous to that of the lactic acids, but more complex, owing to the presence of two asymmetrical atoms in the molecule. The groups are similarly arranged around these two atoms, but in one cyclic sense in the dextro-acid, and in the opposite sense in the lævo-acid; racemic acid being represented by the two formulæ together (§ 141), or simply by the ordinary structural formula. The solid formulæ are in turn represented by plane projections.



Racemic acid is inactive by external compensation, or the mutually opposed action of its active component molecules; it is hence termed an externally compensated compound. The mutually opposed asymmetrical groups of mesotartaric acid must therefore be arranged within the molecule, in such manner that the one active set is neutralised by the other, internally.

Mesotartaric acid being inactive by internal compensation, is termed an internally compensated compound; it is evident that a substance having a single

formula such as this cannot be converted into isomerides without undergoing internal chemical change.

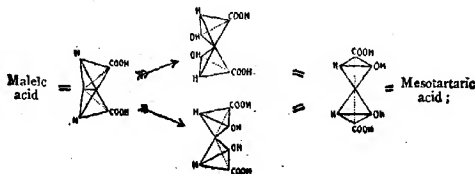


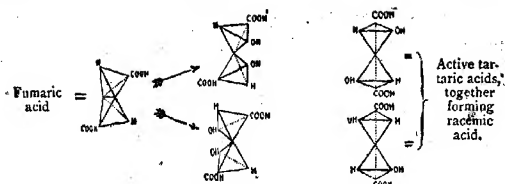
These configurations are confirmed by the chemical relationships of the acids. All four are reduced by hydriodic acid, first to malic acid, and ultimately to succinic acid; but whilst in every case the same succinic acid is produced, the active acids yield the active malic acids, and the inactive acids, inactive malic acid. Similarly, the acids formed by synthetic methods are invariably inactive, the chances of formation of the two active varieties being equal (§ 141).

These formulae also explain the preliminary formation of mesotartaric acid in the racemisation of *d*-tartaric acid. In the dextro-acid both asymmetrical groups are dextrorotatory, and unless both groups in each molecule are inverted simultaneously, which is improbable, the molecules of the initial product each contain one dextrorotatory and one levorotatory group, or are inactive by internal compensation.

But as the inversion proceeds, either the second dextro-groups are converted into laevo-groups, in which case *l*-tartaric acid is formed, or the laevo-groups are reconverted into the original dextro-groups, in which case *d*-tartaric acid is re-formed. There is no selective action in inversions of this kind, and hence the chances are equal; equal numbers of *d*- and *l*-tartaric molecules are produced, and the molecules of the final product each contain one dextrorotatory and one levorotatory molecule, or are inactive by external compensation (compare Synthesis of Lactic Acid, § 141).

The formulae, moreover, are in agreement with those of maleic and fumaric acids. These acids, as ethylene derivatives, are oxidised by dilute permanganate to the corresponding dihydroxy-compounds. But whilst maleic acid is converted into mesotartaric acid, fumaric acid yields only racemic acid, *i.e.* equal quantities of the two active acids (Kekulé, 1880).



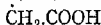


**164. Citric Acid.**—The acid of lemons and sour gooseberries is a hydroxy-polybasic acid, which bears to glycerol a relation somewhat analogous to that of malic acid to glycol, and may be conveniently considered in this place; it is readily obtained from unripe lemons.

The juice having been boiled, and filtered from the coagulated albumen, is neutralised with chalk and milk of lime, and again boiled, the insoluble calcium citrate thus precipitated being decomposed with dilute sulphuric acid, as in the isolation of tartaric acid.



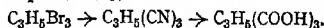
*Citric acid*,  $\text{C}(\text{OH})(\text{COOH}) + \text{H}_2\text{O}$  (Scheele, 1784), forms large



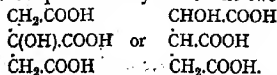
crystals, of pure and very agreeable acid taste; the hydrated acid melts at  $100^\circ$ , and the anhydrous acid at  $153^\circ$ . Citric acid is tribasic, as it forms three classes of salts, such as the *mono*-, *di*- and *tri-potassium citrates*, which are prepared in the same way as the ammonium oxalates (Liebig, 1838); its molecular weight further follows from that of *triethyl citrate*, a liquid boiling at  $185^\circ/17$  mm.

That the acid contains alkylic hydroxyl, is proved by the conversion of this salt by acetyl chloride into *triethyl acetyl-citrate*,  $\text{C}_3\text{H}_5(\text{OAc})(\text{COOEt})_3$ , a crystalline substance, resembling the corresponding tartrate.

As regards nucleal constitution, citric acid is a derivative of glycerol, for it is reduced by hydriodic acid to *tricarballic acid*,  $\text{C}_3\text{H}_5(\text{COOH})_3$ , a soluble crystalline substance melting at  $166^\circ$ , which can be made from tribromhydrin by the cyanide synthesis (Simpson, 1863).



It is therefore represented by one of the two formulae—



The first of these must be chosen, for the acid is oxidised

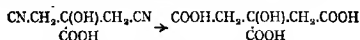
to acetone and carbon dioxide when distilled with manganese dioxide and dilute sulphuric acid; and when heated with concentrated sulphuric acid on a water-bath, it yields carbon monoxide and a crystalline acetone derivative, which separates on slightly diluting the product with water.

*Acetone-dicarboxylic acid*,  $\text{COOH}\cdot\text{CH}_2\cdot\text{CO}\cdot\text{CH}_2\cdot\text{COOH}$  (Pechmann, 1891) is a crystalline substance which melts at  $130^\circ$ , and then decomposes into carbon dioxide and acetone.

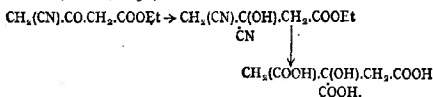


**165. Synthesis of Citric Acid.**—Citric acid can be synthesised both from dichloracetone, and from acetoacetic acid.

*Dichloracetone*,  $\text{CH}_2\text{Cl}\cdot\text{CO}\cdot\text{CH}_2\text{Cl}$ , a crystalline substance formed by oxidising  $\alpha$ -dichlorhydrin with chromic acid, is converted by the cyanhydrin synthesis into *dichloroacetic acid*,  $\text{CH}_2\text{Cl}\cdot\text{C(OH)(COOH)}\cdot\text{CH}_2\text{Cl}$ . This substance is converted into the corresponding *dicyanoacetic acid*,  $\text{CN}\cdot\text{CH}_2\cdot\text{C(OH)(COOH)}\cdot\text{CH}_2\cdot\text{CN}$ , by boiling with concentrated potassium cyanide solution; and on saturating the product with hydrogen chloride, the cyanide is hydrolysed to citric acid (Grimaux, 1880).



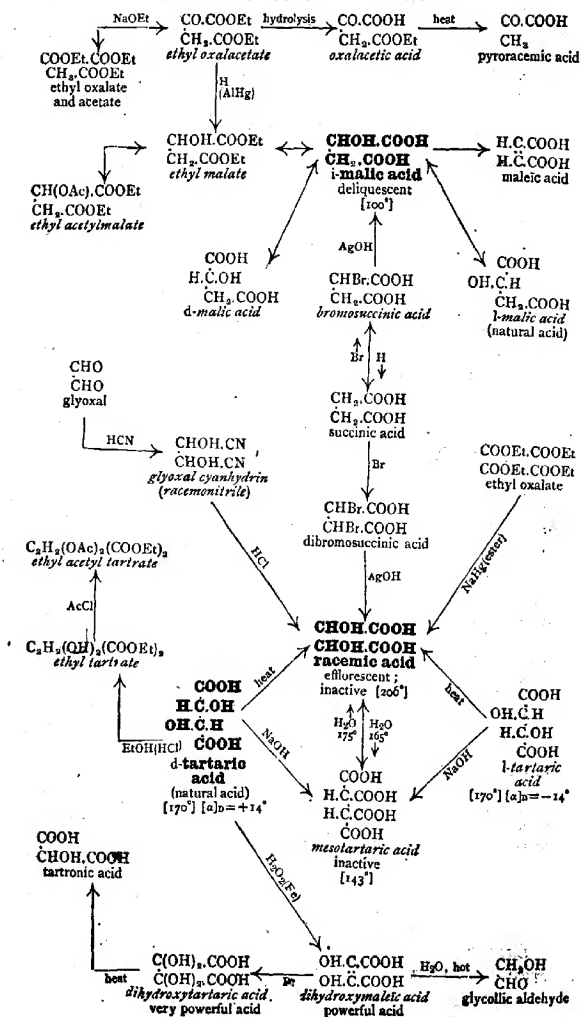
The acetoacetic synthesis is effected by chlorinating ethyl acetoacetate, and heating the  $\gamma$ -chloroacetoacetate,  $\text{CH}_2\text{Cl}\cdot\text{CO}\cdot\text{CH}_2\cdot\text{COOEt}$ , with potassium cyanide solution. On digesting the  $\gamma$ -cyanoacetoacetate,  $\text{CH}_2(\text{CN})\cdot\text{CO}\cdot\text{CH}_2\cdot\text{COOEt}$ , with hydrocyanic and hydrochloric acids, it is converted into citric acid (Haller, 1891).



The formula of citric acid does not contain asymmetrical carbon, and the acid, unlike the other vegetable hydroxy-acids, is therefore optically inactive, and cannot be resolved into active constituents. As a tertiary alcohol, it is broken up by oxidising agents, acetic and oxalic acids being formed.

**166. Synopsis.**—The vegetable acids, malic and tartaric acid, are hydroxy-succinic acids. They are optically active compounds, but whilst there is only one inactive malic acid, there are two inactive tartaric acids, the second of which is accounted for by the mutually compensating action of the two asymmetrical carbon atoms. Citric acid is a hydroxy-tricarboxylic derivative of glycerol.

## THE ALCOHOLIC DIBASIC ACIDS.



## SECTION IX

### SIX-CARBON DERIVATIVES

#### CHAPTER XXX

##### THE CARBOHYDRATES : SUGARS

**167. Cane Sugar.**—The natural sugars and related products are for the most part either substitution derivatives of hexane, or condensation products of such derivatives. The well-known substance, cane sugar, is of great antiquity. Originally introduced from India in the time of Alexander the Great, the sugar-cane gradually spread through Southern Europe; it was introduced into the West Indies in the fifteenth century, soon after the discovery of America. About half the sugar of commerce is obtained from this source, the remainder being made from the sugar maple in North America, and the sugar beet on the Continent.

The process of extraction is much the same in all cases. The sap or juice, which may contain as much as 20 per cent. of sugar, is expressed mechanically, or exhausted with hot water, and boiled down to a thin syrup. The accompanying vegetable acids are then neutralised, and the albumen precipitated, by the addition of milk of lime, the concentration being continued in steam-heated vacuum pans until crystallisation begins.

The crude crystalline product is ordinary brown sugar, and is converted into white sugar by recrystallising and decolorising with animal charcoal. The mother liquor from the brown sugar yields a second crop of still darker crystals, and the residual uncrystallisable syrup is partly used as molasses or treacle, and partly worked up into alcohol—rum.

Commercial cane sugar is a singularly pure product, and probably no other organic compound is prepared on so large a scale and in so pure a state. Ordinary loaf sugar is crystallised quickly, and from hot solutions, whilst sugar candy is prepared by allowing cold syrup to crystallise slowly on nuclei of string; the various brown sugars are simply products more or less contaminated with mother liquor. In the laboratory, sugar is readily extracted from cane or beet by boiling with moderately strong alcohol.

*Cane sugar* or *sucrose*,  $C_{12}H_{22}O_{11}$ , forms transparent, hard crystals, melting at  $160^{\circ}$  (*saccharum*, from Sanscrit = sandy).



The colourless melt does not at once recrystallise on cooling, but remains for a time in a transparent, amorphous condition—barley sugar. At a somewhat higher temperature the sugar is converted into caramel, a dark brown, permanently amorphous substance, which is still soluble in water. Sugar itself is very soluble, forming the well-known sweet syrup, but it is practically insoluble in absolute alcohol. The aqueous solution is strongly dextrogyrate,  $[\alpha]_D = +66^\circ$ , and the concentration of a sugar solution can therefore be estimated polarimetrically (see Glucose, § 168).

When sugar is heated to redness, it swells up and blackens, giving off the characteristic fumes of burnt sugar; it eventually loses most of its hydrogen and oxygen in the form of water, and is converted into charcoal; concentrated sulphuric acid acts in a similar manner, as a mixture of strong syrup with the acid blackens and swells up enormously. The elements being present in the proportion to form water, sugar and similar compounds are known generically as carbohydrates.

Cane sugar is distinguished from other sugars (§ 168 et seq.) by the action of sulphuric acid, and the absence of action with caustic alkalies, alkaline copper tartrate, yeast, and phenyl-hydrazine. When oxidised with nitric acid, it yields principally oxalic acid (§ 122), but tartaric and saccharic acids (§ 181) are also formed.

**168. Glucose.**—Honey, which was known long before cane sugar, slowly deposits, when kept, a sweet crystalline substance which is quite distinct from that of the sugar-cane. The same substance is obtained by concentrating the juice of ripe grapes and other fruit, and can be prepared artificially by hydrolysing cane sugar or starch with dilute acids (hydrogen ions).

On dissolving powdered cane sugar in warm spirit acidified with very dilute hydrochloric acid, a clear syrup is obtained, which after a few days deposits crystals of glucose; the crystallisation can be effected in twenty-four hours if the syrup is sown with a ready-formed crystal of the product.

Similarly, on digesting starch on a water bath with very dilute sulphuric acid, it is dissolved, and after a time entirely converted into this sugar. On removing the acid with powdered chalk, and concentrating the solution, the glucose eventually separates (Kirchhoff, 1811). As in all such cases, the crystallisation is hastened by introducing a ready-formed crystal into the syrup. If anhydrous glucose crystallised from alcoholic solution in used, and the syrup is warmed, anhydrous crystals at once separate.

Glucose is also formed in diabetes, and is excreted actively enormous quantities, sometimes as much as half a kilogram a day, in the urine of persons suffering from that disease.

*Glucose, dextrose, or grape-sugar*,  $C_6H_{12}O_6$  (Glauber, 1660), is a colourless substance, melting at  $146^\circ$ , which crystallises from cold solutions with 1 mol. of water of crystallisation, but from hot solutions or methyl alcohol in the anhydrous state; it is somewhat less sweet than cane sugar.

Like cane sugar, glucose is dextrogyrate,  $[\alpha]_D = +53^\circ$ ; but when freshly dissolved in cold water its activity is much greater, owing to the initial formation of a labile isomeride. This isomeride is converted into the ordinary stable form, slowly at ordinary temperatures, but rapidly when the solution is heated or made slightly alkaline. The rotatory power of a freshly-made solution of glucose therefore diminishes to about half the initial amount, and then remains constant. This phenomenon, which is common amongst the sugars, is known as birotation or mutarotation.

Glucose differs in many respects from cane sugar. It is soluble in alcohol, is not charred by sulphuric acid, and is coloured brown when warmed with caustic soda solution. It strongly reduces ammoniacal silver nitrate and alkaline copper tartrate (§ 159), when warmed with these agents; in the first case metallic silver is deposited in the form of a mirror, and in the second case, the cupric salt is reduced to red cuprous oxide. An emulsion of bismuth hydroxide in caustic soda is similarly reduced to black metallic bismuth when heated with glucose.

The action with copper is quantitative; one molecule of glucose reduces five atoms of the metal, and the amount of sugar in a solution such as urine may be estimated by running it into a known amount of the boiling copper solution until the colour is just discharged (Fehling, 1849).

Glucose is further distinguished from cane sugar in that it is directly fermentable by yeast (§ 172), and when heated on a water-bath with phenyl-hydrazine acetate is converted into a golden-yellow crystalline compound, glucosazone (§ 185). The microscopic appearance of the osazone crystals is very characteristic, and their formation affords a conclusive proof of the presence of glucose in liquids such as urine (Fischer, 1884).

**169. Fructose.**—Besides glucose, honey and grape-juice contain an isomeric sugar, fructose or levulose, which is much more difficult to crystallise. It is also formed in equal amount with glucose, in the hydrolysis of cane-sugar.

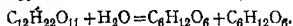
The sugar is hydrolysed by heating on a water bath with dilute sulphuric acid, and the acid is removed with powdered chalk. Slaked lime is now slowly stirred into the ice-cold product without allowing the temperature to rise, and the resulting precipitate of the insoluble lime compound of fructose is filtered off and washed. The precipitate is suspended in water, and washed carbon dioxide passed in until the lime is converted into calcium carbonate; and on evaporating the clear solution, the fructose remains as a syrup (Dubrunfaut, 1848). After dehydrating by shaking with cold absolute alcohol it slowly crystallises, and can then be recrystallised from hot alcohol.

Fructose is also readily obtained in a pure state from inulin or dahlia starch (§ 176), in the same way as glucose from ordinary starch.

*Fructose, levulose or fruit-sugar*,  $C_6H_{12}O_6$  (Lowitz, 1802), is a colourless, crystalline substance melting at  $95^\circ$ . Like cane sugar and glucose, it is optically active, but lævogyrate,  $[\alpha]_D = -71^\circ$ . Fructose reduces metallic salts in the same way as glucose, although more slowly, and it is less easily fermentable by yeast.

On the other hand it is converted by phenyl-hydrazine into glucosazone, and under certain conditions is interconvertible with glucose, and a third isomeric sugar, mannose (§ 186); an alkaline solution of any of these sugars eventually contains all three in equilibrium (de Bruyn, 1895).

The products of the hydrolysis of cane sugar are simply glucose and fructose. The equimolecular mixture, which is obtained in semi-crystalline form on evaporating the product after elimination of the acid, is known as *invert sugar*; the lævo-rotation of the fructose more than counterbalances the dextro-rotation of the glucose, and thus inverts the rotatory power of the cane sugar, the dextrogyrate solution becoming lævogyrate.



**170. Milk Sugar and Malt Sugar : Galactose.**—The sweetness of milk is due to a sugar, milk sugar or lactose, which is isomeric with cane sugar. It is obtained by evaporating clear whey.

*Lactose or milk sugar*,  $C_{12}H_{22}O_{11}$  (Bartoletti, 1619), is a hard, gritty substance, which can be obtained in large crystals, and melts when anhydrous at  $205^\circ$ ; it is less sweet and soluble than cane sugar, but like it is dextrogyrate  $[\alpha]_D = +52^\circ$ .

Lactose is characterised by reducing metallic solutions even in the cold, and forming a yellow osazone; it is not fermentable by yeast, but is converted by the lactic ferment into

lactic acid, which is also formed by fusing it with caustic soda.

Like cane sugar, however, lactose is hydrolysed by dilute mineral acids (although not by weak acids, such as citric acid) to two simpler sugars; one of these is glucose, and the other an isomeric hexose,\* termed galactose.

The lactose is boiled with very dilute sulphuric acid, and the acid eliminated in the manner already described, the new sugar crystallising out from the resulting syrup on adding a crystal of galactose; it is washed with cold alcohol, and recrystallised from boiling alcohol.

*Galactose*,  $C_6H_{12}O_6$  (Erdmann, 1855), is a sweet crystalline substance melting at  $164^\circ$ . It closely resembles glucose, and easily reduces alkaline metallic solutions; but its specific rotatory power is greater,  $[\alpha]_D = +81^\circ$ , and it is practically insoluble in methyl alcohol.

The conversion of starch into glucose is preceded by the formation of a third isomeric cane sugar, which is readily prepared by the action of the enzyme, maltase (§ 173) of malt extract.

A mixture of malt extract with 20 per cent. starch paste is heated at  $60^\circ$  for an hour, and then boiled and filtered; the solution is evaporated to a syrup, and the sugar crystallised from hot methyl alcohol.

*Maltose* or *starch sugar*,  $C_{12}H_{22}O_{11} + H_2O$  (Kirchhoff, 1811), is a crystalline substance somewhat resembling glucose. The anhydrous substance, obtained by drying the hydrated sugar at  $100^\circ$ , is very hygroscopic.

Maltose is strongly dextrogyrate,  $[\alpha]_D = +141^\circ$ , but it is less easily soluble in alcohol, and reduces alkaline metallic solutions less easily than glucose. It forms a characteristic osazone, and is directly fermentable by yeast; when boiled with very dilute sulphuric acid, it is hydrolysed to glucose alone.



A fourth sugar of the same type as cane sugar and lactose, although more complex, is found in eucalyptus manna, and in beet molasses. *Rafinose*,  $C_{15}H_{27}O_{16}$ , is a crystalline substance, which is hydrolysed by dilute sulphuric acid to glucose, fructose and galactose.

171. *The Glucosides*.—A variety of crystalline substances occur in plants, which are hydrolysed by accompanying

\* The difficulty which arises from the use of the word *glucose* as a generic name for six-carbon sugars, as well as a synonym for dextrose, is met by adopting the term *hexose* for the class (Fischer, 1890).

enzymes (§ 173) to glucose and various products, and are termed on this account the glucosides. *Amygdalin*,  $C_{20}H_{27}NO_{11}$ , a soluble crystalline substance, melting at  $200^{\circ}$ , found in bitter almonds, is hydrolysed by the enzyme *emulsin*, or by very dilute sulphuric acid, to grape sugar, benzaldehyde (§ 275) and hydrocyanic acid; it is on account of the formation of the latter that bitter almonds are poisonous.

*Phloridzin*,  $C_{21}H_{24}O_{10}$ , a similar crystalline substance, is formed in the root bark of apple and other trees of the same order, and is hydrolysed by acids to glucose, phloretic acid and phloroglucinol (§ 305); it is of interest as producing artificial diabetes in animals. *Potassium myronate*,  $C_{16}H_{18}KO_6NS_2$ , the crystalline glucoside of black mustard seed, is hydrolysed by alkalis, or the accompanying enzyme *myrosin*, to glucose, allyl mustard oil (§ 210), and potassium hydrogen sulphate.

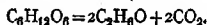
Some of the glucosides can be made synthetically. *Helicin*,  $C_{13}H_{16}O_6$ , a glucoside obtained by the oxidation of *salicin*, the natural glucoside of the willow (§ 308), can be synthesised from salicylic aldehyde and glucose; when reduced with sodium amalgam it is reconverted into salicin, identical with the natural product. Analogous but simpler compounds, such as the *methyl-glucosides*,  $C_6H_{11}O_6\text{OME}$ , have been formed by saturating alcoholic solutions of glucose with hydrogen chloride.

**172. Fermentation.**—The various processes of fermentation which are so frequently used in preparing organic substances consist essentially in decomposing them by means of certain microscopic fungi, or rather, by the action of complex albuminous substances, termed *enzymes*, which are secreted by these fungoid organisms.

The alcoholic fermentation of glucose, fructose and maltose is induced by the enzyme *zymase* (§ 173) of the yeast fungus, a minute, widely distributed, unicellular organism.

The action only proceeds within certain limits of temperature,  $4\text{--}34^{\circ}$  and most quickly within much narrower limits,  $25\text{--}30^{\circ}$ , and in solutions of appropriate concentration; it stops as soon as a certain percentage of alcohol is formed, the fungus being killed by strong alcohol, as well as by heat and acids, and the ordinary antiseptics; certain mineral and ammonium salts must also be present to afford food for the ferment.

The greater part of the sugar (95 per cent.) is converted into alcohol and carbon dioxide, the latter gas being evolved in abundance. The decomposition is apparently simple,\* and is of historical interest, as the equation of weight between the sugar and the resulting products afforded the first instance of the law of conservation of mass (Lavoisier, 1790).



\* It is possible, however, that lactic acid is an intermediate product.

The residue of the sugar is converted into glycerol (3 per cent.), succinic acid (0.5 per cent.), and fusel oil, the constituents of which, as already incidentally stated, are mainly isopropyl, isobutyl, isoamyl, and active amyl alcohols, together with normal propyl and butyl and higher alcohols. The formation of these compounds is due to the presence of foreign organisms, as their amount diminishes as the yeast is freed from such impurities by selective cultivation.

The lactic fermentation of sugar and the destruction of tartaric acid by mould are effected by similar organisms, and the natural oxidation of alcohol to acetic acid is brought about by a fungus, *mycoderma aceti*, which will thrive even in a 14 per cent. solution of alcohol. Similarly urea in urine (§ 191) is hydrolysed by *micrococcus ureæ*; putrefaction itself is due to the action of such ferments, the ptomaines or animal alkaloids (§ 215) being formed in this manner from albumen and other proteins (§ 222).

The action of the yeast enzymes, in conjunction with that of diastase (§ 173), is utilised in brewing and spirit-making. After the starch of the grain has been hydrolysed to maltose by the diastase of the malt, yeast is added to the warm mash, and as soon as enough of the maltose and dextrin (§ 177) has been converted into alcohol, is separated mechanically. The product is then flavoured with hops, and coloured if necessary with charred malt. Beer rarely contains more than 5 per cent. of alcohol.

In the manufacture of grain spirits, such as whisky, the product is distilled without the addition of hops or colouring matter. In the preparation of potato spirit much the same procedure is followed, but the hydrolysis of the starch is partially effected by steaming the potatoes under pressure at 150°, before adding the water and malt. In making potato-spirit, pure cultivated yeast is usually employed.

**178. Enzymes.**—Whilst little is yet known of the chemical mechanism of fermentation, it is certain that the change is not dependent on "vital" action, but is due to the action, catalytic or otherwise, of *enzymes*—non-living, albuminous substances of complex constitution, which are secreted by the living ferment-organisms, but retain their activity under conditions which are incompatible with life.

It has been known for many years that germinating seeds contain an enzyme, diastase, by which starch is rapidly hydrolysed to maltose. This enzyme is present in relatively large amount in malt, and is obtained as a gelatinous precipitate on adding alcohol to malt extract.\* The precipitated

\* Malt is barley which has been soaked until germination commences,

diastase can be washed with alcohol and ether, and dried on a porous plate without impairing its activity.

*Diastase* (Payen, 1833) is a white amorphous powder, which dissolves in water to a clear solution, and like albumen, is coagulated by heat. When a little diastase is added to warm starch emulsion, the jelly liquefies with great rapidity, and the starch is eventually hydrolysed to maltose.

Saliva contains a similar enzyme, *ptyalin*, which hydrolyses the starch of food in a similar manner, and thus prepares it for assimilation. Milk sugar is similarly hydrolysed to its constituents by an enzyme, *lactase*, which is present in milk.

The enzymes of yeast are of great practical importance. By extracting powdered yeast with water, a solution is obtained from which an enzyme, maltase, is precipitated by alcohol.

*Maltase* rapidly hydrolyses maltose to glucose, and the action is quantitative when the solution is dilute; it has no action on cane-sugar or milk-sugar.

In concentrated solutions the process is reversed, and the glucose is condensed to maltose and isomeric sugars; equilibrium results in a 40 per cent. solution of either sugar when 84 per cent. of the maltose has been hydrolysed, or 16 per cent. of the glucose condensed. This reciprocal action is termed reversible zymolysis (Croft Hill, 1894).

If pressed yeast be kept for some weeks, it does not putrefy, but is converted into a yellow liquid, termed yeast liquor, from which, after due filtration, a second enzyme, invertase, is precipitated by alcohol.

*Invertase* is a soluble, albuminous substance resembling maltase. When added to warm cane-sugar solution it inverts (hydrolyses) the sugar with great rapidity; the action is catalytic, as the enzyme can afterwards be precipitated unchanged. Invertase is coagulated at 65°, and destroyed by alkalis.

The alcoholic fermentation of sugar is caused by an enzyme, *zymase*, which can be extracted in a similar manner after the yeast cells have been ruptured by prolonged grinding with fine quartz sand; the fragments of the cells are removed by filtration through porous porcelain under pressure.

*Zymase* (Buchner, 1897) is an albuminous substance, which

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and then heated or "malted" to destroy the living germ; the diastase remains unaffected, and not only hydrolyses the starch of the malt itself, but also that of the unmalted grain which is mashed up with the malt in the process of brewing.

resembles its congeners; when it is added to warm glucose solution a brisk effervescence immediately commences, owing to the resolution of the sugar into alcohol and carbon dioxide. As zymase usually contains invertase, it also ferments cane-sugar solution with equal rapidity.

The activity of these enzymes is suspended at low temperatures, or in presence of much alcohol, and is destroyed by heat and most chemical agents\*; prussic acid immediately "poisons" zymase, as if it were a living organism.

**174. Selective Action of Enzymes.**—The action of enzymes is governed largely by stereochemical conditions. The molecules of the various hexoses contain four asymmetrical carbon atoms, and the possibilities of stereoisomerism are therefore very great. Yeast attacks those sugars with greatest readiness whose configuration or spacial constitution most closely resembles that of grape-sugar, and leaves the antipodal compounds practically unaffected. It hydrolyses dextro-methyl- $\alpha$ -glucoside (§§ 171, 181) but not the corresponding laevo-compound; it ferments the sugars containing three, six or nine-carbon atoms in the molecule, but leaves the four, five and seven-carbon sugars untouched.

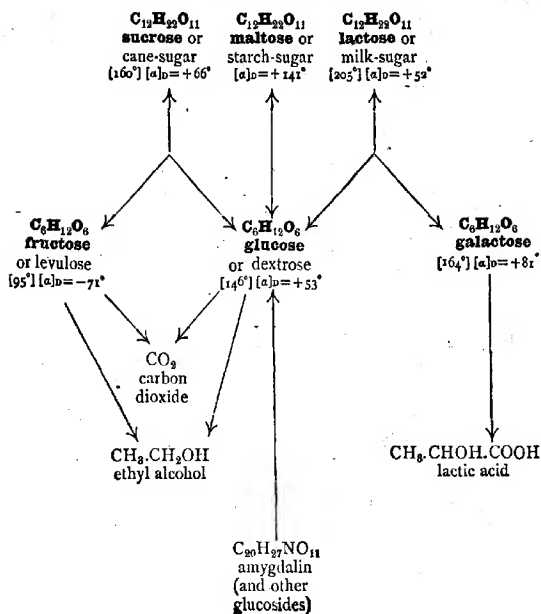
An analogous phenomenon obtains in the esterification of mandelic acid (§ 282) by an optically active alcohol, laevo-menthol (§ 349); mandelic acid is a racemic compound, and on heating it with the alcohol the dextro-acid is converted into ester, the laevo-acid remaining unaffected (Marckwald, 1899). The separation of "racemic" acids as salts of optically active alkaloids (§ 162) is due to a similar cause. The enzymes have not yet been isolated in a pure state, but they are known to be optically active like albumen (§ 222), and it seems probable that just as a key can only turn the corresponding lock, an enzyme can only decompose a substance of similar molecular configuration (Fischer, 1899).

**175. Synopsis.**—The natural sugars are six-carbon or twelve-carbon saturated compounds. They are termed carbohydrates as they contain hydrogen and oxygen in the proportion to form water. The twelve-carbon sugars or hexabioses are hydrolysed by very dilute acids and enzymes to the six-carbon sugars or hexamonomes, and the latter are split up in various ways by similar ferments. The most important decomposition of this class is that of glucose and fructose into alcohol and carbon dioxide by an enzyme zymase, secreted by the yeast fungus.

\* The activity of enzymes appears also to be dependent on the presence of a co-ferment. The co-ferment of zymase is a dialysable and non-coagulable substance, which is soluble in water, and insoluble in alcohol, and may be separated from the enzyme by filtration through gelatine (Harden, 1904). Neither zymase nor its co-ferment alone produces fermentation of glucose, which proceeds only in presence of both.



## THE NATURAL SUGARS.



## CHAPTER XXXI

### THE CARBOHYDRATES: STARCH AND CELLULOSE

**176. The Starches.**—From the ready manner in which glucose and maltose are prepared from ordinary starch, and fructose from inulin, it is obvious that the starches are very closely related to the sugars. Like the latter they are carbohydrates.

The starches are the reserve material of plants, and are probably formed from the sugars when the amount of the latter synthesised by the plant is in excess of immediate requirements. Bulbs and tubers contain large quantities of starch, and this is why bulbous plants can grow and mature at a much earlier period of the year than others. Seeds contain only enough for the development of the seed-leaves.

Starch is usually obtained from grain or potatoes. When a stiff paste of wheaten flour is tied up in a cotton bag, and kneaded under cold water the finely divided starch passes through the fabric, leaving the gluten and other constituents of the flour behind, and on keeping the milky liquid the starch gradually subsides, and may be dried at the ordinary temperature. It is separated on a manufacturing scale on much the same plan, the interstitial material being previously softened and disintegrated by allowing the coarsely-crushed and moistened grain to ferment.

*Starch* or *amylum*,  $(C_{12}H_{20}O_{10})_x$ , is a white, pulverulent substance, which has been known from very early times (*αμυλον* = unground [flour]). It consists of amorphous, microscopic granules, of characteristic shape, usually oval or circular, although sometimes angular. These granules are composed of concentric layers, showing organised structure, and vary in size from 0.002 mm. in rice and pepper to as much as 0.1 mm. in sago and potato starch.

Starch granules are quite insoluble in cold water and alcohol, but they are converted by boiling water into an opalescent, sticky paste or emulsion. The starch is, in fact, resolved into two constituents, an insoluble *starch cellulose* (compare Cellulose, § 178), which constitutes the outer layers

of the granules, and a soluble starch or granulose, which forms the nuclei (Naegeli, 1856); the granulose is precipitated on the addition of alcohol to the clear filtered solution.

*Granulose* or *soluble starch*,  $(C_{12}H_{20}O_{10})_{100}$ \* is a tasteless, granular substance, which is readily soluble in water, but insoluble in alcohol. Like the sugars into which it is convertible, it is strongly dextrogyrate,  $[\alpha]_D = +200^\circ$ , and is blackened by sulphuric acid; but it does not reduce Fehling's solution, nor yield an osazone with phenylhydrazine.

Granulose is characterised by forming with cold iodine solutions an unstable additive *iodine compound*, having an intensely blue colour, which is temporarily discharged by heat.

Other starches are known, but all have the same empirical formula. *Glycogen* or *animal starch* (Bernard, 1857) is found in the livers of animals, in which it is probably stored as a reserve material for use in periods of fasting; it is converted by ferments into maltose, and by dilute acids directly into glucose; and it differs from ordinary starches in that it is coloured red by iodine. *Inulin*,  $C_{72}H_{124}O_{62}$ , the starch of dahlia and like tubers, is coloured yellow by iodine, and is quantitatively hydrolysed to fructose by dilute acids.

**177. The Dextrins and Gums.**—The ultimate product of the hydrolysis of starch is either maltose or glucose, as the hydrolytic agent is malt or a dilute acid; but several intermediate compounds, which are formed concurrently with the maltose, can be isolated during the process by fractional precipitation with alcohol. They are similarly produced when starch is heated at  $200^\circ$  (Vauquelin, 1811), and on account of their high dextrorotatory power are termed the dextrins.

These compounds, which are polymeric with starch, are transparent, amorphous substances, devoid of taste or odour; they are freely soluble in water, forming sticky, gummy solutions which are used as substitutes for natural gum; the gloss produced on starched fabrics by ironing is due to the formation of transparent dextrins.

The dextrins are readily isolated by precipitation with alcohol, in which they are insoluble, and they are sharply distinguished from starch by their behaviour with iodine, with which they either give a red colour or no colour at all.

The higher dextrins are optically nearly as active as starch, and have

\* The molecular weights of the compounds of the starch group have been determined approximately by the cryoscopic method, and from their hydrolytic decompositions.

very little reducing power, but as the series is descended and the molecular weight diminishes, the rotatory power falls off and the reducing power increases, until at last these constants approximate to those of maltose. It is therefore possible that there is only one dextrin, which has the same rotatory power as starch, the reducing products precipitated by alcohol from the products of starch hydrolysis being compounds of this with maltose. Some of these products, however, are very well defined.

*Erythrodextrin*,  $(C_{12}H_{20}O_{10})_8 + H_2O$ , of which at least two varieties can be isolated, is a soluble, gummy substance, which is precipitated by alcohol in spheroidal crystals. It is strongly dextrogyrate,  $[\alpha]_D = +196^\circ$ , but differs from granulose in that it is coloured red by iodine (whence its name) and reduces Fehling's solution.

*Maltodextrin* or *achroodextrin*,  $(C_{12}H_{20}O_{10})_3 + H_2O$ , is a sweetish, soluble substance, which differs from granulose and erythrodextrin in that it is not coloured by iodine. Its rotatory power is less,  $[\alpha]_D = +182^\circ$ , and it reduces Fehling's solution about two-thirds as strongly as maltose. Maltodextrin is hydrolysed to maltose by diastase, and to glucose by dilute acids; at least four varieties have been isolated.

The natural gums are probably sugar condensation products allied to the dextrins. The principal constituent of gum arabic is the calcium salt of *arabic acid*,  $(C_8H_{10}O_6)_n$ , an acid which is isomeric with starch and the dextrins, and yields galactose on hydrolysis. Other gums are hydrolysable to five-carbon sugars (§ 188); cherry gum yields arabinose, and beech gum, xylose.

**178. The Celluloses.**—The cell walls of plants are composed of a carbohydrate termed cellulose, which is isomeric with starch, and closely related to the sugars. Simple cell aggregates, such as cotton and flax, consist almost entirely of this substance, whilst even in complex structures, such as wood, in which the chains of cells are cemented together by interstitial material, it forms the chief constituent.

The isolation of cellulose from cotton and the like is simple. The Swedish filter paper made from linen rags is almost pure cellulose, and after dissolving out the small amount of iron and lime salts and silica, with hydrochloric and hydrofluoric acids, leaves practically no ash.

Wood cellulose is more difficult to isolate, the interstitial material having to be dissolved out. In the manufacture of wood pulp, the chopped wood is digested with caustic soda solution, at a high temperature and under pressure; in some processes, to avoid loss by oxidation, acid sulphites are used, such as those of lime or magnesia. By the end of the operation the wood is reduced to a soft grey pulp, which, after washing with water and bleaching with ordinary bleaching solution without addition of acid, is fairly pure cellulose.

**Cellulose**,  $(C_{12}H_{20}O_{10})_x$ , is a white substance which is insoluble in all ordinary solvents, but dissolves freely in an ammoniacal solution of copper oxide (Schweizer's reagent). When simply isolated from cotton or wood, it retains the tubular structure of the cell (the product from coniferous wood shows the characteristic pits); but when reprecipitated from the copper solution with dilute acids, it forms a colourless jelly, which dries to a horny amorphous mass.

On immersing cellulose in slightly diluted sulphuric acid it quickly swells up and becomes transparent, and is eventually disintegrated; but if paper thus treated is quickly washed while the action is yet superficial, and before disintegration has commenced, it is converted into a tough impermeable substance, known as *vegetable parchment*. By diluting the sulphuric acid solution of the cellulose immediately after disintegration, a gelatinous isomeric substance is obtained which forms a blue iodide, and hence is known as *amyloid*.

By prolonged digestion with concentrated sulphuric acid cellulose is converted into *sulphates*, which are hydrolysed to glucose on boiling with water; it is thus a derivative of glucose, so that alcohol and its numerous derivatives may be made from sawdust and rags (Braconnot, 1811).

It will be seen later that the carbohydrates are complex alcoholic substances, and form salts with acids in the same way as glycerol; *pentacetylcellulose*,  $[C_6H_5(OAc)_5]_x$ , is thus formed from cellulose and acetic anhydride. The cellulose nitrates, which are made by digesting cellulose with a mixture of nitric and sulphuric acids, in the same way as glycerol nitrate, are of great importance, both as explosives, and as plastic materials.

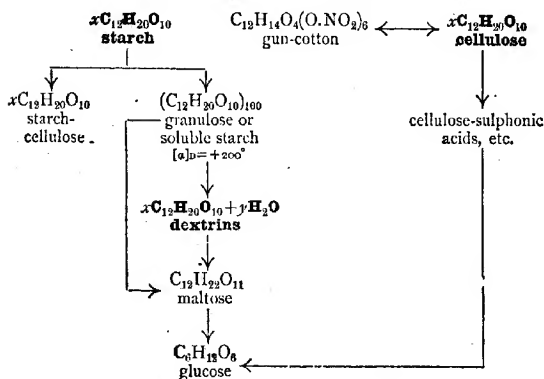
*Cellulose hexanitrate* or *gun-cotton*,  $C_{12}H_{14}O_4(O.NO_2)_6$  (Schönbein, 1846), is made by immersing dry cotton wool, which has previously been washed with potassium carbonate solution and water, in a mixture of nitric acid with three times its volume of concentrated sulphuric acid. The product, which retains the form and appearance of the cotton, is thoroughly washed with water—on the large scale, in a pulp-washing engine—and dried in air.

Gun-cotton burns quickly but quietly in the open-air, but when detonated in a confined space explodes with great violence. It partially dissolves in nitroglycerine to a gelatinous mass, which, when mixed with castor-oil as a moderant, or with vaseline as a lubricant, forms a valuable "high" explosive, termed *maximite* or *cordite*; this is now used instead of gunpowder, as it is smokeless.

Cellulose hexanitrate is insoluble in alcohol-ether, but by digesting the cellulose for many hours with a large excess of the mixed acids, a soluble *pentanitrate* is formed. The solution of this, which is termed *collodion*, is used in photography and surgery, as it leaves a thin waterproof film of the nitrate on any surface to which it is applied. A mixture of camphor and collodion-cotton is the "*celluloid*," of which imitations of starched linen, ivory, and tortoiseshell are made; it burns with almost-explosive violence when ignited.

**179. Synopsis.**—The starches and celluloses are insoluble or partially soluble carbohydrates, which are ultimately converted into glucose by hydrolytic agents. The gums are probably intermediate products. The nitrates of cellulose are used as explosives, and in photography.

#### STARCH AND CELLULOSE.

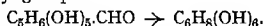


## CHAPTER XXXII

### THE CONSTITUTION OF THE SUGARS

**180. Reduction of Glucose to Sorbitol and Hexane.**—In its power of reducing metals, glucose resembles the aldehydes and hydroxy-acids; it is not an acid, however, for although it forms compounds with metallic oxides, such as *calcium oxide glucose*,  $C_6H_{12}O_6 \cdot CaO$ , these compounds are additive.

As it forms a crystalline *oxime*, and, under certain conditions, a *hydrazone*, it is an aldehyde or ketone; and that it is also a pentatomic alcohol is proved by its conversion into crystalline *pentacetyl-glucose* when acetylated. Its aldehydic character is further confirmed by its reduction by sodium amalgam to an alcohol, sorbitol, the molecule of which contains six hydroxyl groups.



*Sorbitol*,  $C_6H_8(OH)_6$ , is a crystalline substance, melting at  $108^\circ$ , which occurs naturally in the sap of the mountain ash; the presence of the six hydroxyl groups shows that it is a hexahydroxy-hexane, and it is in fact convertible into *n*-hexane.

When repeatedly distilled with fuming hydriodic acid and red phosphorus, sorbitol is converted into a *secondary hexyl iodide*,  $C_6H_{13}I$ , boiling at  $167^\circ$ ; and this is converted into normal hexane by simple reduction with zinc and hydrochloric acid. The hydrocarbon is identical with that which may be isolated from light petroleum, or made synthetically by the action of sodium on normal propyl iodide.

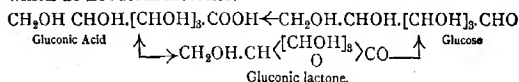
Sorbitol is therefore a *normal hexahydroxyhexane*, and as it is a stable compound, and can even be distilled unchanged under very low pressure, it follows that the six hydroxyl groups are attached to six different carbon atoms. It is thus the six-carbon analogue of glycerol, and its conversion into secondary hexyl iodide is parallel to that of glycerol into isopropyl iodide.



**181. Oxidation of Glucose : its Constitution.**—Glucose is thus either the aldehyde, or one of the two possible ketonic derivatives of sorbitol. On oxidising it in the cold with bromine water, it is converted into an acid containing the same number of carbon atoms, from which it may again be formed by indirect reduction ; the first view must therefore be adopted.

*Gluconic acid*,  $\text{CH}_2\text{OH}.\text{[CHOH]}_4.\text{COOH}$ , is a syrupy substance, which, like sorbitol and unlike glucose, does not reduce metallic solutions. It cannot itself be crystallised, as on concentrating its solution it is dehydrated to *gluconic lactone*, which crystallises on further concentration (compare § 151).

On reducing gluconic lactone with sodium amalgam in slightly acid solution it is reconverted into glucose (Fischer, 1889). This is an action of great synthetic importance ; the acid itself is not reduced in this manner, nor are acids like tartaric acid which do not form lactones.



Gluconic acid is readily separated from other substances by means of its phenyl-hydrazide. *Gluconic phenylhydrazide*,  $\text{CH}_2\text{OH}.\text{[CHOH]}_4.\text{CO}.\text{NH.NHPh}$  (Fischer, 1889), is a crystalline substance melting at  $200^\circ$ , which is prepared by heating the acid or lactone with phenyl-hydrazine and dilute acetic acid on a water-bath. When heated with strong baryta-water it is hydrolysed to phenylhydrazine, which can be extracted with ether, and barium gluconate, from which the acid is set free by dilute sulphuric acid ; the hydrazides resemble the amides in character.

On oxidising gluconic acid with dilute nitric acid, it is converted into saccharic acid, which may be made in the same way from cane sugar and glucose.

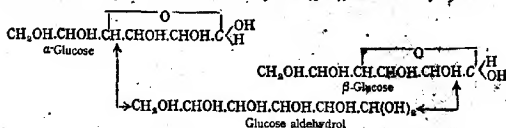
Either of these sugars is warmed with excess of moderately concentrated nitric acid, not above  $60^\circ$ , until fumes cease to be evolved ; the solution is slightly diluted, the accompanying oxalic acid is allowed to crystallise out, and the product is neutralised with potassium carbonate, and strongly acidified with acetic acid ; after some days, potassium hydrogen saccharate separates.

*Saccharic acid*,  $\text{COOH}.\text{[CHOH]}_4.\text{COOH}$ , is a deliquescent, gummy substance, which like gluconic acid readily forms a lactone. It is a dibasic acid, and its constitution is further proved by its reduction to adipic acid,  $\text{COOH}.\text{[CH}_2\text{]}_4.\text{COOH}$  (§ 152), when heated with hydriodic acid and red phosphorus. By further oxidation with nitric acid it is converted into tartaric and oxalic acids





to  $\alpha$ - and  $\beta$ -glucose, which are therefore similarly constituted to them; the interconvertibility of the sugars is probably due to the alternate formation and dehydration of an aldehydrol (§ 84) or other hydrate.



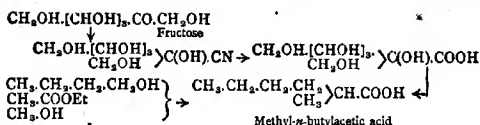
**182. Constitution of Fructose: Mannitol.**—Like glucose, fructose reduces alkaline metallic solutions, and forms compounds with metallic oxides. It also forms an *oxime* and a crystalline *pentacetyl derivative*, and that it is an aldehyde or ketone is confirmed by its reduction to an alcohol, mannitol, which is stereoisomeric with sorbitol.

The hexahydroxy-hexanes contain four asymmetrical carbon atoms, and their isomerism is therefore very complicated; eight optically active and two inactive compounds are possible, and most of them are known. Mannitol is the principal constituent of the common manna of the manna ash, from which it is readily obtained in a pure state by recrystallisation from hot dilute alcohol.

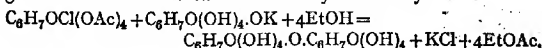
**Mannitol**,  $\text{CH}_2\text{OH}(\text{CHOH})_4\text{CH}_2\text{OH}$  (Proust, 1806), is a sweet substance, which forms large crystals, melting at  $166^\circ$ . It forms a *hexacetate*, and is converted by hydriodic acid, etc., into a hexyl iodide and hexane identical with those obtained from sorbitol; but it is not itself identical with sorbitol, as its melting point and oxidation products are different.

Although the actions of fructose closely resemble those of glucose, its behaviour on oxidation is very different; it is broken up even by mild oxidising agents, and oxalic and mesotartaric acids are the first isolable products. A ketone of the constitution,  $\text{CH}_2\text{OH}[\text{CHOH}]_3\text{CO}.\text{CH}_2\text{OH}$ , might be expected to break up in this manner, in the same way as methyl butyl ketone breaks up into acetic and butyric acids; and that fructose is this ketone is proved by the cyanhydrin synthesis, in the same way as with glucose.

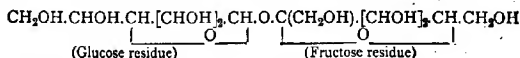
**Fructose cyanhydrin** (Killiani, 1885), a crystalline substance, melting at  $115^\circ$ , is converted by hydrolytic agents into a lactone, in the same way as glucose cyanhydrin; this lactone is reduced by hydriodic acid and phosphorus to a heptylic acid, whose boiling point and salts are identical with those of *methyl-n-butyl-acetic acid*,  $\text{CHMeBu}.\text{COOH}$ , made by the acetoacetic synthesis. Fructose or levulose is thus a ketone derived from the hexatomic alcohol mannitol (Killiani, 1886).



**183. Constitution of the Complex Carbohydrates.**—Cane sugar can be made artificially by digesting potassium fructose in alcoholic solution with *acetyl-chlorhydrase*, a compound which is formed by the action of acetyl chloride on glucose (Marchlewski, 1896); and, as will be seen in the next chapter, both glucose and fructose can be made synthetically.



Cane sugar forms an *octacetyl derivative*, and as it does not reduce metallic solutions, nor form an osazone, the remaining three oxygen atoms can only function in ethereal combination. The following formula, amongst others, epitomises these relations (Fischer; compare Methylglucosides, § 181).

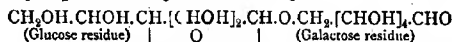


Milk sugar and malt sugar are also octohydroxy-compounds, but they reduce metals and form osazones. That they are aldehydic and not ketonic is proved by their oxidation by bromine water to monocarboxylic acids containing the same number of carbon atoms.

*Lactobionic acid*,  $\text{C}_{12}\text{H}_{21}\text{O}_{10} \cdot \text{COOH}$ , the first oxidation product of lactose, is hydrolysed by acids to glucose and galactonic acid, an acid which is stereoisomeric with gluconic acid, and is formed by oxidising galactose with bromine water.

Galactose is an aldose stereoisomeric with glucose. It is reducible to an alcohol, *dulcitol*, which is stereoisomeric with mannitol and sorbitol, and the *galactonic acid*, which is formed from it by oxidation with bromine water is further oxidised by nitric acid to *mucic acid*, a stereoisomeride of saccharic acid. Mucic acid, like saccharic acid, is reduced to adipic acid when heated with hydriodic acid and phosphorus.

The constitution of lactose, as *galactose-glucoside* (§ 181), is probably represented by the following formula.



Maltose or *glucose-glucoside* is stereoisomeric with lactose.

**184. Synopsis.**—The six-carbon sugars are aldehydic or ketonic derivatives of normal hexahydroxyhexane.



## CHAPTER XXXIII

### SYNTHESIS OF THE SUGARS

**185. Glucosazone : Conversion of Glucose into Fructose.**—When glucose is heated on a water-bath for half an hour with phenyl hydrazine acetate, the whole of the sugar is precipitated in the form of glucosazone ; if the original solutions are clear, this only needs washing with water and drying, but otherwise it must be recrystallised from hot alcohol.

Fructose yields identically the same compound, and the osazone is best made in quantity from invert sugar, formed by heating cane-sugar solution on a water-bath for an hour with a little dilute sulphuric acid ; the mineral acid must be neutralised before adding the hydrazine.

*Phenyl-glucosazone*,  $\text{CH}_2\text{OH} \cdot [\text{CHOH}]_3 \cdot \text{C}(\text{:N.NHPh}) \cdot \text{CH:N.NHPh}$  (Fischer, 1884), is a golden-yellow crystalline substance, melting at  $204^\circ$  ; its constitution follows from the manner of its formation and hydrolysis.

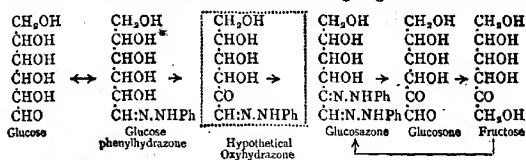
When warmed with concentrated hydrochloric acid for a minute, phenyl glucosazone is completely hydrolysed, and in the course of half an hour at the ordinary temperature a quantity of phenyl-hydrazine hydrochloride crystallises out. On neutralising the ice-cold and diluted solution with lead carbonate, a lead compound is obtained from which a sweet fermentable substance, glucosone, is set free by dilute sulphuric acid.

*Glucosone* or *oxyglucose*,  $\text{CH}_2\text{OH} \cdot [\text{CHOH}]_3 \cdot \text{CO} \cdot \text{CHO}$  (Fischer, 1888), is an exceedingly soluble substance, which has not been crystallised ; but that it is both a ketone and an aldehyde is proved by its immediate conversion into glucosazone when mixed with phenyl-hydrazine acetate solution, and by its reduction to fructose by zinc dust and acetic acid.

In this way the aldehyde sugar or aldose may be converted into the ketonic sugar or ketose. The reverse transformation may also be effected, but by a circuitous method, through mannonic and gluconic acids (§ 186).

The conversion of glucose and fructose into glucosazone is due to the oxidation of one of the alcohol groups by a third molecule of phenyl-hydrazine, which is reduced to ammonia

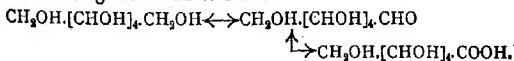
and aniline (§ 249). All sugars which reduce metallic solutions form such osazones, but the non-reducing sugars do not do so.



**186. Mannose and Mannonic Acid.**—When mannitol is warmed with dilute nitric acid it is partly oxidised to fructose, but partly also to mannose, an aldose or aldehyde-sugar stereoisomeric with glucose; the oxidation is more readily effected by means of hydrogen peroxide in presence of ferrous iron, and in this case mannose alone is formed (Fenton, 1898). Mannose can also be obtained in quantity by hydrolysing vegetable ivory with dilute sulphuric acid (Fischer, 1889).

Mannose is readily separated from the ketonic sugar by adding phenylhydrazine acetate to the cold neutralised solution; a dense yellow precipitate of *mannose phenyl-hydrazone* separates, from which the sugar can be recovered by hydrolysis with dilute hydrochloric acid, in much the same way as gluconic acid from its hydrazide (§ 181).

*Mannose*,  $\text{CH}_2\text{OH}[\text{CHOH}]_4\text{CHO}$  (Gorup-Besanez, 1861), is a sweet substance, melting at  $136^\circ$ , which resembles glucose in almost every respect, except that it is more strongly dextrogyrate. On further oxidation with bromine, etc., it yields *mannonic* and *mannosaccharic acids*, compounds which closely resemble and are stereoisomeric with gluconic and saccharic acids. Conversely, *mannonic lactone* is reduced by sodium amalgam to mannose and mannitol, in the same way as gluconic lactone to glucose and sorbitol.



Mannose and mannonic acid are very intimately related to fructose, glucose and gluconic acid; mannosazone is identical with glucosazone and fructosazone; mannose, fructose and glucose are partially interconvertible in alkaline solution (§ 169); and mannonic and gluconic acids are similarly interconvertible. When mannonic acid is heated with excess of moist quinoline (§ 385) for an hour at  $140^\circ$ , it is partially converted into gluconic acid, and vice versa.

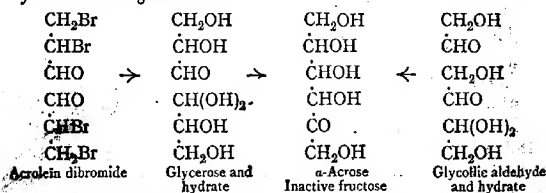
The two acids are separated by fractionally crystallising their brucine salts; the product is made alkaline with baryta, the liberated quinoline distilled off with steam, and the barium exactly precipitated with dilute sulphuric acid; the hot concentrated solution of the mixed acids is then saturated with brucine (§ 402), and on allowing it to crystallise, *brucine mannonate* separates. The brucine is precipitated with baryta from the residual solution of *brucine gluconate*, and the metal eliminated as before; the gluconic acid is then isolated from the product in the form of its hydrazide, and from this the lactone can be made in the manner described above (§ 181).

As gluconic lactone is reducible to glucose, it follows that the latter can be made from mannonic acid, and thus from fructose. This is an important step in the synthesis of the sugars.

**187. Synthesis of Glucose and Fructose.**—Formaldehyde and metaformaldehyde polymerise to sugars when digested with lime water, and the same action occurs under various conditions with glycollic and glyceric aldehydes, both of which, like formaldehyde, have a "carbohydrate" formula. Until the osazones were discovered, it was not possible to isolate and examine these synthetic sugars, and beyond the fact that they reduce metallic solutions, and in general behave like glucose (Butlerow, 1861), little was known about them.

The synthetic sugar first thoroughly examined was obtained from acrolein dibromide, and subsequently also from formaldehyde and glyceraldehyde. The product obtained by the hydrolysis of acrolein dibromide yields with phenylhydrazine not the osazone of glycerose but that of its polymeride  $\alpha$ -acrose. The same product is obtained by heating glycollic aldehyde, with which it is also polymeric.

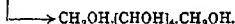
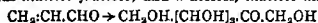
$\alpha$ -Acrose is *inactive fructose*, and condenses with phenylhydrazine to *i*-glucosazone.



$\alpha$ -Acrosazone is extremely like glucosazone, but like all synthetic products is optically inactive. It melts at  $205^\circ$ , and is converted by hydrochloric acid into  $\alpha$ -acrosone, a syrupy liquid resembling glucosone. This, when digested with zinc dust and acetic acid, is reconverted into  $\alpha$ -acrose.

$\alpha$ -Acrose (Fischer, 1887) is therefore a ketonic sugar; the product thus

purified is in fact very like fructose, but optically inactive. By further reduction with sodium amalgam it is converted into *α-acritol*, an inactive isomeride of mannitol and sorbitol. That it is a "racemic" compound is proved by fermenting it with yeast; the ordinary fructose, to which the yeast is accustomed (§ 174), is destroyed, and the solution becomes dextrogyrate from the liberation of the oppositely active isomeride. *α-Acrose* is thus *inactive fructose*, and *α-acritol*, *inactive mannitol*.

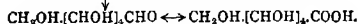
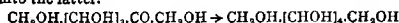


As this alcohol is inactive mannitol, it should be oxidisable to a "racemic" mannonic acid. The oxidation is in fact effected in the same way as with mannitol, by the successive action of dilute nitric acid and bromine water. By concentrating the solution of the strychnine salt of inactive mannonic acid, *strychnine lavomannonate* separates, whilst by converting the mother liquor into the morphine salt, and again concentrating, *morphine dextromannonate* is obtained.

The dextromannonate yields *d-mannonic acid*, which is identical with the mannonic acid from mannose, whilst the lavomannonate yields the antipodal *l-mannonic acid*, the rotatory powers of the two acids being equal and opposite.

Conversely, the active acids can be reconverted into the inactive acids, in the same way as with the lactic and tartaric acids. *Lavomannonic acid* can be obtained in quantity from a five-carbon sugar, arabinose (§ 188), by the cyanhydrin synthesis; on mixing a solution of its lactone with that of an equal weight of ordinary mannolactone, an inactive acid and lactone are obtained, which are identical with those formed by oxidation of *α-acritol*, and are reducible by sodium amalgam to an *inactive mannose* and *inactive mannitol*. The latter is identical with *α-acritol*.

There is no doubt, therefore, that the synthetic mannonic acid is the racemic compound corresponding with the ordinary acid, and can be resolved into the latter.



As mannonic acid is convertible into gluconic acid, glucose and fructose (§ 186), the synthetic chain between glycerol and these natural sugars is complete.\* The validity of the synthesis rests on the identity of the two acids and alcohols, for owing to secondary actions, the yield of *α-acrose* is so small (the acrolein from a kilogram of glycerol yields only 18 grams of *α-acrosazone*), that it would be impracticable actually to convert glycerol into glucose. As previously explained in connexion with the cyanide synthesis, this is immaterial.

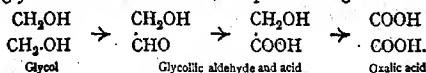
**188. Synthesis of the Aldoses.**—All the lower paraffins are connected with polyalcohols, aldoses, etc., in the same way as hexane with glucose and mannitol; the prototype of the glucose-saccharic series is the glycol-oxalic series.

Glycollic aldehyde behaves in every respect as a true sugar; it is a carbohydrate, is sweet like sugar, reduces metallic

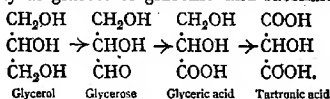
\* See Chart at end of chapter.



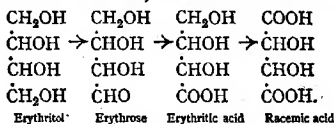
solutions, and forms an osazone; it is itself reducible to an alcohol, glycol, and oxidisable to mono- and di-carboxylic acids, glycollic and oxalic acids; the parallel to glucose is exact.



Glyceric aldehyde or glycerose has the same properties, and undergoes the same transformations; it forms an *oxime* and a yellow crystalline *osazone*, analogous to glucosazone; it is reducible to glycerol, in the same way as glucose to sorbitol, and is oxidisable to glyceric and tartronic acids, in the same way as glucose to gluconic and saccharic acids.



In the four-carbon series, the compounds are physically like the hexane sugars. *Erythritol*,  $\text{CH}_2\text{OH}.\text{CHOH}.\text{CHOH}.\text{CH}_2\text{OH}$  (Stenhouse, 1848), is a crystalline substance resembling mannitol, and melting at  $126^\circ$ ; it is found in combination in certain lichens. It is oxidised by hydrogen peroxide in presence of ferrous iron to *erythrose*,  $\text{CH}_2\text{OH}.\text{CHOH}.\text{CHOH}.\text{CHO}$ , a four-carbon syrupy sugar, which is convertible by bromine water and nitric acid into *erythritic acid* and racemic acid.



Several stereoisomeric five-carbon series are known. *Lavo-arabinose*,  $\text{CH}_2\text{OH}.[\text{CHOH}]_3.\text{CHO}$ , a sugar obtained by hydrolysis of gum arabic and other gums, is a sweet crystalline substance, melting at  $160^\circ$ ; that it is an aldehyde is proved by its conversion into a mixture of levomannonic and levogluconic acids by the cyanhydrin synthesis. It is reduced by sodium amalgam to *lavoarabitol*, a sweet crystalline substance resembling mannitol, and is oxidised by bromine water and nitric acid to *lavoarabonic acid* and *trihydroxyglutaric acid*.

Eight stereoisomeric pentaldoses and pentonic acids are possible. *Xylose*, an aldose obtained by hydrolysis of beech gum or straw, is one of the *lactose pentoses*. It is converted by the cyanhydrin synthesis into a

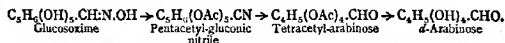
mixture of *levo-gulonic* and *levo-idonic* acids, which are stereoisomeric with gluconic and mannonic acids, and the first of which is reducible to sorbitol. All the pentaldoses condense to furfuraldehyde (§ 407) when distilled with dilute hydrochloric acid.

Heptane, octane, and nonane aldoses, alcohols and acids have also been made by successive steps from the hexoses by means of the cyanhydrin synthesis, in the same way as the hexoses from the pentoses (Fischer). *Mannoheptitol*,  $\text{CH}_2\text{OH} \cdot [\text{CHOH}]_5 \cdot \text{CH}_2\text{OH}$ , is identical with the perseitol of the Persian laurel; it is reduced to tetrahydrotoluene (§ 290) when heated with hydriodic acid.

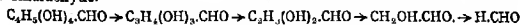
**188. Degradation of the Aldoses.**—The process of building up the higher sugars from the lower sugars is reversible, and the higher sugars may be degraded step by step until formaldehyde is reached. The degradation is effected either by means of the oximes of the sugars, or by the action of hydrogen peroxide on the acids in presence of ferric iron.

*Glucosoxime*,  $\text{C}_6\text{H}_9(\text{OH})_5 \cdot \text{CH}:\text{N} \cdot \text{OH}$ , a crystalline substance melting at  $137^\circ$ , is made by adding finely-powdered glucose to a boiling alcoholic solution of hydroxylamine (hydroxylamine hydrochloride and soda); when it is heated with acetic anhydride and sodium acetate, there is a violent action, and on mixing the product with water crystals of *pent-acetylgluconic nitrile* separate, the aldoxime losing a molecule of water and at the same time undergoing acetylation.

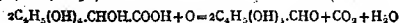
This nitrile is identical with the pentacetyl compound of *d-arabinose-cyanhydrin*, and like all cyanhydrins loses hydrogen cyanide when warmed with ammoniacal silver nitrate, leaving the aldehyde, *tetracetyl-d-arabinose*. The acetyl groups may now be removed by hydrolysis, leaving *d-arabinose* itself, as may be proved by converting it into its osazone. The hexose, glucose, is thus degraded to the pentose, arabinose (Wohl, 1893).



In the same way arabinose can be degraded to tetrose, tetrose to glycero, glycerose to glycollic aldehyde, and finally, glycollic aldehyde to formaldehyde.

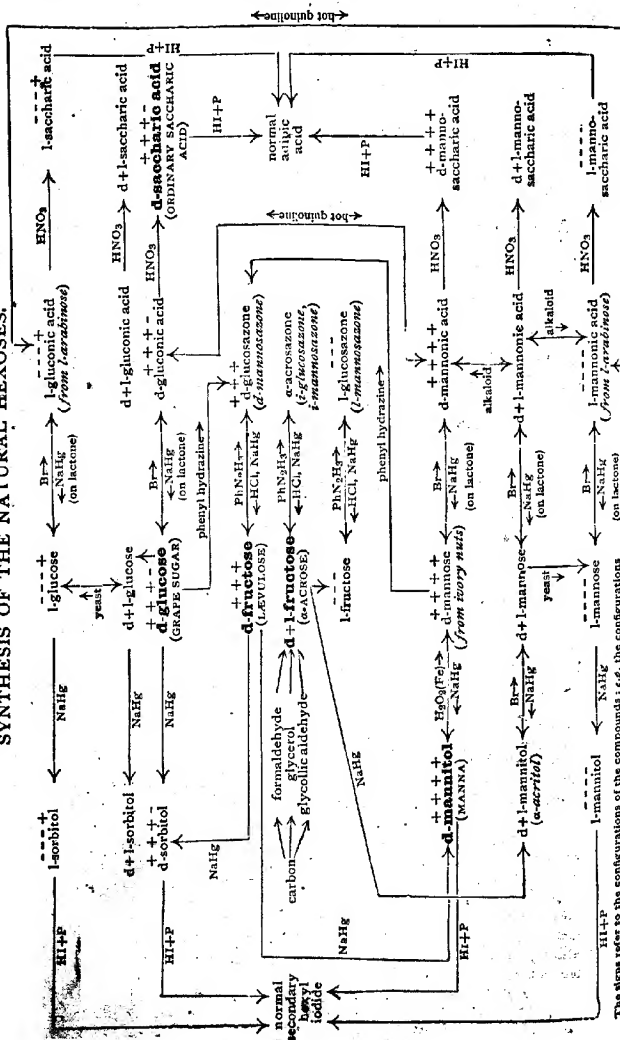


The degradation of the acids is dependent on the fact that their calcium salts are oxidised to the next lower aldoses by hydrogen peroxide in presence of ferric iron, whilst the aldoses are unaffected by this agent. When calcium gluconate is digested with hydrogen peroxide and basic ferric acetate, *d-arabinose* and calcium carbonate are formed; the iron and excess of hydrogen peroxide are removed by adding manganese dioxide, and the sugar is isolated by means of its oxime, from which the osazone may be obtained by heating with phenylhydrazine. Gluconic acid can thus be degraded to the same arabinose from which it is made synthetically (Ruff, 1898).



**190. Synopses.**—Glucose, fructose and various isomeric sugars can be made synthetically by polymerisation of lower aldehydes, and can be reconverted into them by degradation. Owing to the presence of four asymmetrical carbon atoms their isomerism is very complex.

## SYNTHESIS OF THE NATURAL HEXOSES.



The signs refer to the configurations of the compounds: e.g. the configurations

## SECTION X

### ALIPHATIC DERIVATIVES OF NITROGEN, ETC.

#### CHAPTER XXXIV

##### CARBAMIDE

**191. Urea or Carbamide.**—The chief classes of oxygenated aliphatic compounds have now been dealt with, and the only group remaining to be considered, before passing on to derivatives of other hydrocarbons, is one comprising a number of compounds in which nitrogen, or in some cases other elements, plays the predominant part. Some of these compounds, such as the simple amides and amines, and the nitriles, have already been discussed incidentally, but there are others more complex, which need further consideration.

The first of these are the complex amides of carbonic acid, which are substances of great physiological importance. The waste nitrogen of mammals is excreted in the urine, partly in the form of uric acid and allied compounds, but mainly in that of a basic substance, urea or carbamide. This base is readily separated from fresh urine.

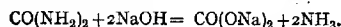
The liquid is evaporated on a water-bath, and on adding an equal bulk of concentrated nitric acid to the cooled, thin syrup, it immediately becomes semi-solid from the separation of *urea nitrate*, a crystalline substance which is insoluble in nitric acid. The nitrate is purified by dissolving in warm water to which animal charcoal is added, to remove the pigment, and is then reprecipitated with nitric acid. The base is now set free by adding barium carbonate to the aqueous solution as long as effervescence occurs; the urea carbonate, which might be expected, is too unstable to exist, and consequently on evaporating the product to dryness on a water-bath, a mixture of urea with barium nitrate and excess of carbonate is obtained. The urea is extracted from this with hot absolute alcohol, in which barium nitrate is insoluble, and readily crystallises on distilling off the solvent. It is more economically prepared synthetically from potassium cyanide (§ 192).



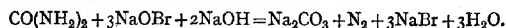
*Urea* or *carbamide*,  $\text{CO}(\text{NH}_2)_2$ , (Rouelle, 1773), forms long transparent prisms, resembling nitre in taste; it melts at  $132^\circ$ , and is freely soluble in water and alcohol. It is but a feeble, monacid base, and forms stable salts only with the stronger acids; *urea nitrate* is soluble in water, but insoluble in nitric acid, and hence serves for the isolation of the base; *urea oxalate* is a similar, but sparingly soluble salt. In aqueous solution these salts are hydrolytically dissociated into urea and free acid, so that their solutions are always strongly acid.

Urea also forms compounds with salts; *sodium chloride urea*,  $\text{CON}_2\text{H}_4\text{NaCl}\cdot\text{H}_2\text{O}$ , is a crystalline substance; *mercuric nitrate urea*,  $\text{CON}_2\text{H}_4\cdot\text{HgO}\cdot\text{Hg}(\text{NO}_3)_2$ , is an insoluble, basic substance, which is precipitated on adding mercuric nitrate to a solution of the base, and is sometimes used for its detection and estimation.

Urea thus resembles the amides in its chemical behaviour, and that it is the amide of carbonic acid is proved by boiling it with very concentrated caustic soda, when it is hydrolysed to ammonia and sodium carbonate. A similar decomposition is effected naturally in the early stages of the putrefaction of urine, the urea being hydrated to ammonium carbonate by a microbe, *micrococcus ureæ*.

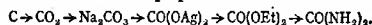


The derivation of urea from ammonia is shown, moreover, by the action of nitrous acid, which converts it into carbon dioxide and nitrogen in the normal manner. The same decomposition is effected by sodium hypobromite, and the amount of urea in urine may be approximately estimated by measuring the nitrogen thus liberated from a known volume of the liquid; the hypobromite is made at the time by adding bromine to cooled caustic soda solution.



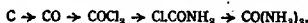
**192. Synthesis of Urea.**—The constitution of urea, as determined by these analytical methods, is confirmed by various syntheses from carbonic acid derivatives.

It is formed by heating ammonia with ethyl carbonate, the action being the same as that involved in the preparation of oxamide from ethyl oxalate.

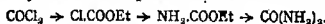


It is also obtained by the direct action of ammonia on *carbonyl chloride* or *phosgene*, an easily condensable gas, which is formed by oxidising chlorine with chromic acid, or by direct union of carbon monoxide with chlorine in sunlight; it is most conveniently prepared by heating carbon tetrachloride with pyrosulphuric acid. The formation of carbamide from

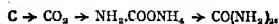
carbonyl chloride is parallel to the formation of acetamide from acetyl chloride, with the exception that an intermediate compound, *chloro-formamide*,  $\text{Cl.CONH}_2$ , is produced; this may be obtained as a very volatile crystalline solid by passing carbonyl chloride over heated ammonium chloride.



Urea is also obtained by the action of ammonia on *ethyl chlorocarbonate* or *chloroformate*,  $\text{Cl.CO.OEt}$ , a liquid which is formed, together with ethyl carbonate, by heating an alcoholic solution of phosgene gas; a very soluble crystalline substance, *ethyl carbamate* or *urethane*,  $\text{NH}_2\text{.CO.OEt}$ , analogous to ethyl oxamate, is produced in the first instance.



The corresponding *ammonium carbamate* or "sesquicarbonate," which is formed by the direct union of carbon dioxide and ammonia, is also convertible into urea, as it loses water when heated, in the same way as ammonium acetate; a similar synthesis of carbamide from ammonium carbonate is believed to be effected in the liver.

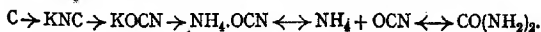


These syntheses render it clear that urea is the diamide of carbonic acid. They are not adapted for the preparation of the substance, however, and it is best made in quantity from ammonium cyanate, with which it is isomeric.

Solid ammonium cyanate (§ 207), is at once transformed into urea when warmed; in aqueous solution the action is reversible, equilibrium resulting when about 95 per cent. of the cyanate ions have been converted into urea, or five per cent. of the urea into cyanate ions (Walker, 1895).\*

The ammonium cyanate is conveniently made from potassium cyanate, which is prepared from the cyanide, either by fusing it with red lead or some similar oxidising agent, or by oxidising it in cold aqueous solution with alkaline permanganate. In the lead process, the cyanide is fused with excess of litharge or red lead, and on evaporating the solution of the potassium cyanate with the equivalent amount of ammonium sulphate, a residue of potassium sulphate and urea is left.

Much of the potassium sulphate crystallises out as the solution is concentrated, and the urea is separated from the remainder by extracting the dry product with hot strong alcohol, in which the sulphate is insoluble; traces of red and blue colouring matters are usually also formed.



The cyanide synthesis of urea is of peculiar interest, as it was the first synthesis of an Organic compound effected (Wöh-

\* Hence unless special precautions are taken, the results obtained in the hypobromite estimation of urea are too low.

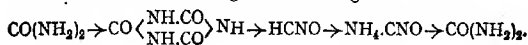
ler, 1828). Previously to this, and even long afterwards, it was maintained that the action of living organisms was essential to the formation of Organic compounds. This view has long been abandoned, but it is still held by many that "organised" or "living" matter is fundamentally different from that which is made in the laboratory.

**193. Condensation Products of Urea.**—When urea is heated it loses ammonia, and passes through a characteristic cycle of changes. The first product, *biuret* or *allophanamide*,  $\text{NH}_2\text{CO.NH.CO.NH}_2$  (Liebig and Wöhler, 1834), a crystalline substance melting at  $190^\circ$ , is also formed by heating ammonia with *ethyl allophanate*,  $\text{NH}_2\text{CO.NH.COOEt}$ , a substance which is formed synthetically by the action of carbamide on ethyl chlorocarbonate. Biuret is distinguished by the formation of a violet colour when dilute copper sulphate is added to its solution in caustic soda.

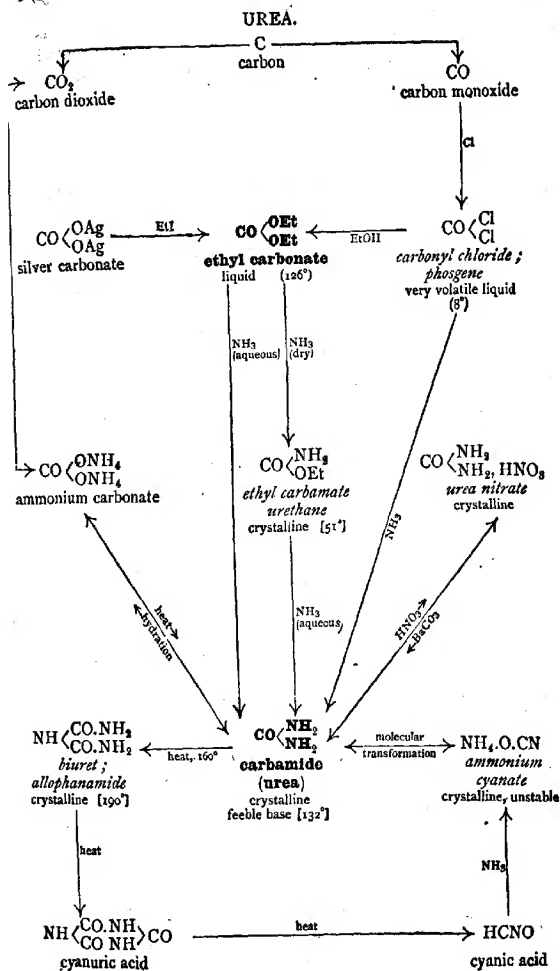


By further heating carbamide or biuret, more ammonia is lost, and *cyanuric acid*,  $\text{C}_3\text{H}_3\text{N}_3\text{O}_3$ , a white crystalline substance is formed; it is more readily prepared by dissolving urea in dilute hydrochloric acid, and heating the evaporated residue as long as heavy fumes of ammonium chloride are given off. Cyanuric acid is converted into a characteristic insoluble, crystalline barium salt, when barium chloride is added to its solution in dilute ammonia, and thus serves for the detection of urea.

When cyanuric acid is heated to dull redness, it is converted into cyanic acid,  $\text{HCNO}$  (§ 208), by the addition of aqueous ammonia to which the original urea is again obtained.



**194. Synopsis.**—Urea or carbamide, the principal constituent of mammalian urine, is the diamide of carbonic acid.





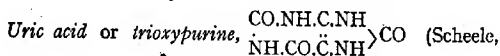
## CHAPTER XXXV

### THE PURINE GROUP

**195. Uric Acid.**—Whilst urea is the principal constituent of mammalian urine, the urine of birds and reptiles contains a large proportion of uric acid. Snakes' excrement consists of fairly pure ammonium urate, and affords a convenient source of the acid.

The excrement is boiled with dilute caustic soda until ammonia ceases to be evolved, and the uric acid is precipitated from the clear hot sodium urate solution by pouring it into excess of cold dilute hydrochloric acid. The product is dissolved in warm concentrated sulphuric acid, and reprecipitated by water, and the uric acid thus purified is washed with water and dried.

The acid can be precipitated from human urine by acidifying it with hydrochloric acid, or better, by saturating it with ammonium chloride, when ammonium hydrogen urate is thrown down quantitatively (Hopkins, 1892). The latter is then treated in the same way as the snakes' excrement.

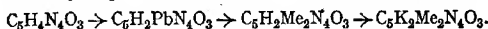


is a white microcrystalline powder, which is very sparingly soluble in water; although the solution is slightly acid to litmus, the acidity is so feeble \* that uric acid is entirely precipitated from its solution by dilute mineral acids. The molecular weight of uric acid is determined by the cryoscopic method, from its solution in monohydrated sulphuric acid (this can be frozen in ice and salt).

Uric acid is a feeble dibasic acid, and forms salts such as *potassium urate*,  $\text{C}_5\text{H}_3\text{KN}_4\text{O}_3$ , and *dipotassium urate*,  $\text{C}_5\text{H}_2\text{K}_2\text{N}_4\text{O}_3$ , but the latter is decomposed even by carbon dioxide. By heating lead urate with methyl iodide, it is converted into *dimethyluric acid*,  $\text{C}_5\text{H}_3\text{Me}_2\text{N}_4\text{O}_3$ , a crystalline substance which

\*  $K = 0.0000015$   
260

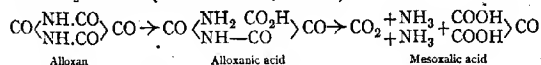
resembles uric acid and is also a dibasic acid; further, *tetra-methyluric acid*,  $C_6Me_4N_4O_3$ , is formed directly by shaking a cold alkaline solution of sodium urate (uric acid in concentrated caustic soda) with methyl iodide. It thus follows that all four hydrogen atoms of the uric acid molecule are acid.



**196. The Ureides.**—Uric acid is readily convertible into acidyl derivatives of urea, which are analogous to the amides, and are hence termed the *ureides*. When the pure acid is added in small portions to moderately concentrated nitric acid, it dissolves with gentle effervescence, owing to the evolution of carbon dioxide and nitrogen. If the action is moderated, by cooling if necessary, and no nitrous fumes are evolved, crystals of a new substance, alloxan, begin to appear after a certain amount of the acid has been dissolved.

The solution may now be warmed, but not above  $50^\circ$ , and more acid dissolved, and on finally cooling, the alloxan separates in quantity. It is drained on an asbestos filter, and after washing with a little ice-water, is recrystallized from the minimum amount of warm water. Several further crops can be obtained by dissolving more acid in the mother liquor.

*Alloxan* or *mesoxalyl urea*,  $CO \begin{smallmatrix} NH.CO \\ NH.CO \end{smallmatrix} C(OH)_2 + 3H_2O$  (Brugnatelli, 1817), is a crystalline, efflorescent, semi-acid substance, which stains the skin red, and gives it a heavy, sickly odour. When boiled with caustic baryta, it is hydrolysed, first to *alloxanic acid*, and finally to mesoxalic acid, carbon dioxide and ammonia, whence its constitution. On account of the instability of mesoxalic acid, alloxan cannot be made by direct synthesis (see Allantoïn, below.)



As a ketone, alloxan forms a crystalline bisulphite compound, and its relation to mesoxalic acid is further shown by the tenacity with which it retains the fourth molecule of water. Three molecules separate at  $100^\circ$  in the ordinary manner, but the fourth is lost only at  $150^\circ$ ; the carboxyl groups have the same influence as the chlorine in chloral hydrate.

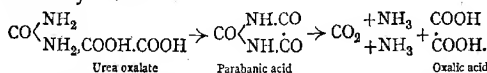
Alloxan forms an unstable, deep-blue compound with ferrous salts, and is reduced by sulphuretted hydrogen, etc., to *alloxantin*,  $[CO : (NH.CO)_2 : C(OH)_2]$ , a colourless, sparingly soluble substance, which is converted by ammonia into *murexide*, a purple dye; this was much used before the introduction of the synthetic coal-tar dyes. Some *alloxantin* is always formed in the preparation of alloxan, or it may be

obtained directly from uric acid by using a milder oxidising agent, such as potassium chlorate and hydrochloric acid. If a little uric acid or urate be evaporated to dryness in a porcelain dish with a few drops of nitric acid, an orange-red residue is obtained, from which the purple murexide is at once produced by moistening with cold ammonia; this is a delicate test for compounds of the uric acid group.

When alloxan is heated with excess of concentrated nitric acid at 70°, carbon dioxide is evolved, and on concentrating and cooling the product, a second oxidation product crystallises out; it may be recrystallised from water.

*Parabanic acid* or *oxalyl urea*  $\text{CO}:(\text{NH})_2:\text{C}_2\text{O}_2$  (Liebig and Wöhler, 1838), is a soluble crystalline substance, which is strongly acid to litmus. It is a dibasic acid, the hydrogen of the imido-groups being acid as in succinimide, owing to the juxtaposition of the carbonyl group; the *silver salt*,  $\text{CO}:(\text{NAg})_2:\text{C}_2\text{O}_2$ , is obtained as a crystalline precipitate on adding silver nitrate to a solution of the acid.

That parabanic acid is the ureide of oxalic acid is shown analytically by its hydrolysis to ammonia and sodium oxalate and carbonate when heated with caustic soda, and synthetically, by its formation when urea oxalate is warmed with phosphorus oxychloride.

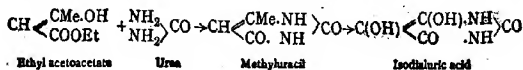


Parabanic acid is quite stable towards acids, but it is partially hydrolysed by bases. Thus on neutralising a warm solution of the acid with ammonia, *ammonium oxalurate*,  $\text{NH}_2\text{CO.NH.CO.COONH}_4$ , crystallises out on cooling. Acids such as *alloxanic acid* and *oxaluric acid* are termed *ureide acids*; they are strong acids.

On adding lead peroxide to boiling water in which uric acid is suspended, the ureide is converted into urea, and a third oxidation product, allantoin, which crystallises out after removing the accompanying lead oxalate and carbonate; the urea separates on further concentrating the mother-liquor.

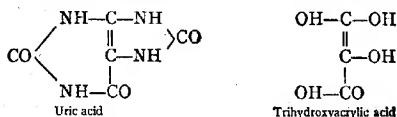
*Allantoin* or *glyoxylic diureide*,  $\text{CO} \begin{array}{c} \text{NH} \cdot \text{CH} \cdot \text{NH} \\ \diagup \quad \diagdown \\ \text{NH} \cdot \text{CO} \quad \text{NH}_2 \end{array} \text{CO}$ , is a neutral crystalline substance, which is readily soluble in alcohol and hot water; it occurs naturally in the allantoin fluid of the cow, and may be made synthetically by heating glyoxylic or mesoxalic acid with urea at 100°.

*Methyluracil* or *acetoacetic ureide* is similarly made by condensing urea with ethyl acetoacetate (§ 144); it is convertible by a complex process of oxidation into *isodaluric acid*, which in turn condenses with urea in presence of hot sulphuric acid, forming uric acid (§ 197).

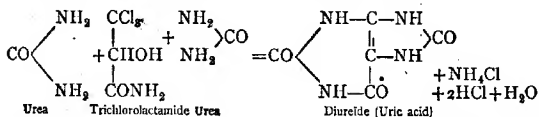


**197. Constitution and Synthesis of Uric Acid : Purine.**—As uric acid is convertible into alloxan and urea, its molecule presumably contains the nuclei of both these substances; and as all four hydrogen atoms are replaceable by metal, the probability is that these are linked to the nitrogen atoms as in alloxan. That this is actually so, is proved by the elimination of the whole of the nitrogen as methylamine, when tetramethyluric acid is hydrolysed with concentrated hydrochloric acid at  $70^{\circ}$ ; no ammonia is formed (Fischer, 1884).

From these and other considerations it follows that uric acid is the diureide of trihydroxyacrylic acid (Medicus, 1875).



This formula is borne out by the synthetic relations of the acid. Trihydroxyacrylic acid is as yet unknown, but small quantities of uric acid are formed by heating urea with the chemically equivalent *trichlorolactamide*, a substance which is made from chloral cyanhydrin (Horbaczewski, 1887).



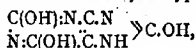
More complicated syntheses affording better yields have been effected by means of isodialuric acid (Behrend, 1888; § 196), and malonic acid (Fischer, 1895; see Caffeine, § 199). The first synthesis of the acid was effected by heating urea with glycine (§ 217), and was suggested by the reduction of the acid to glycine, carbon dioxide and ammonia, when heated with hydriodic acid (Horbaczewski, 1883).

When uric acid is heated with phosphorus oxychloride at  $160^{\circ}$ , it is converted into *trichloropurine*,  $\text{CCl}:\text{N}:\text{C}:\text{N} \begin{smallmatrix} \diagup \\ \diagdown \end{smallmatrix} \text{CCl}$ , a crystalline acid substance melting at  $189^{\circ}$ ; this compound by successive reduction with hydriodic acid and zinc dust is converted into purine, the mother-substance of the uric acid group.

*Purine*,  $\text{CH}:\text{N}:\text{C}:\text{N} \begin{smallmatrix} \diagup \\ \diagdown \end{smallmatrix} \text{CH}$  (Fischer, 1897), is a well-defined, crystalline

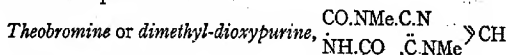
substance melting at  $217^{\circ}$ ; it has both acid and basic properties, and forms a *zinc salt*, as well as a *nitrate* and a *picrate*.

Uric acid is the stable form of *trihydroxypurine*,



and is hence termed *trioxypurine*. The relation between uric acid and trihydroxypurine is analogous to that between the ketonic and enolic forms of ethyl acetoacetate (§ 144).

**198. Theobromine and Caffeine.**—The active principles of tea, coffee and cocoa are two basic substances, which are closely related to uric acid. Theobromine, the active alkaloid of cocoa, is readily extracted from powdered cocoa beans by boiling them with water; the tannin, etc., is precipitated from the infusion with lead acetate, and after removing the lead with hydrogen sulphide, the theobromine is extracted with alcohol from the evaporated residue.

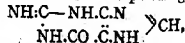


(Woskresensky, 1842), is a bitter, crystalline powder, which can be sublimed unchanged. Theobromine forms salts with acids, as well as with metals; its molecular formula as a monacid base follows from the analysis of its platinichloride. Its relation to uric acid is indicated by its oxidation by nascent chlorine to methyl-alloxan and methyl-urea (Fischer, 1882), and confirmed by its synthetic relations to xanthine, caffeine, and uric acid.



is a white amorphous substance, which occurs in the animal organism and in tea.

It is best prepared by the action of nitrous acid on the corresponding imido-compound, *guanine* or *imido-oxy-purine*,



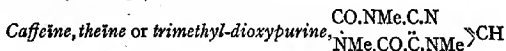
a base which occurs in guano. Both guanine and xanthine are oxidised by nascent chlorine in the same way as theobromine, and therefore also contain the uric acid nucleus; guanine yields guanidine (§ 227), together with parabanic acid and carbon dioxide—the oxidation products of alloxan; xanthine yields urea and alloxan itself.

Xanthine is a semi-acid substance, like uric acid, and when its lead salt is heated with methyl iodide is converted into *dimethylxanthine* (Fischer, 1882), which is identical with *theobromine*. Similarly, when silver theobromine is heated

with methyl iodide, it is converted into methyl-theobromine or trimethylxanthine, a base which is identical with caffeine or theine, the alkaloid of tea and coffee (Strecker, 1861).

Caffeine is best extracted from tea, but is physiologically and chemically identical with the product prepared in a similar manner from coffee.

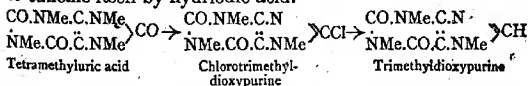
The tea is thoroughly boiled with water, and the tannin and albuminous matter are precipitated by treating the hot solution with basic lead acetate, the excess of which is then removed by adding the exact amount of dilute sulphuric acid. The solution is concentrated and the caffeine extracted by shaking it with chloroform.



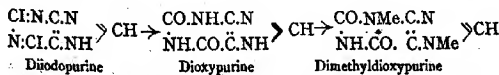
(Runge, 1829), is a silky, crystalline substance, which melts at  $233^\circ$ . Its constitution as a member of the uric acid group is established, independently of its formation from xanthine and theobromine, by its oxidation by nascent chlorine to dimethyl-alloxan and methyl-urea, and by synthesis.

The presence of three methyl groups linked to nitrogen is also independently proved by its quantitative hydrolysis by concentrated hydrochloric acid at  $250^\circ$ , to carbonic and formic acids, ammonia, methylamine and sarcosine (§ 218).

**199. Synthesis of Theobromine and Caffeine.**—Caffeine is readily formed from uric acid. On heating the crystalline tetramethyl derivative of the latter (§ 195) with phosphorus oxychloride, it is converted into *chlorocaffeine*, which is reduced to caffeine itself by hydriodic acid.



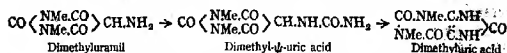
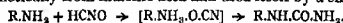
Caffeine and theobromine may also be synthesised through xanthine, which is formed synthetically when *di-iodopurine*, the crystalline intermediate product in the reduction of trichloropurine to purine (§ 197), is hydrolysed with hydrochloric acid at  $100^\circ$ .



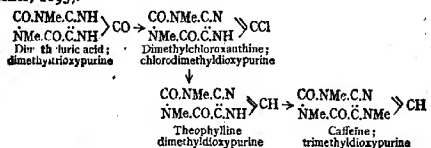
Uric acid and caffeine may be directly synthesised from malonic acid and urea or *s*-dimethylurea (§ 207). When malonic acid and dimethylurea are heated together with phosphorus oxychloride, they condense to

*malonyl-dimethylurea*,  $\text{CH}_2:(\text{CO.NMe})_2:\text{CO}$ , a ureide which contains the alloxan nucleus, and is converted into *dimethylalloxan-oxime*,  $\text{OH.N:C}:(\text{CO.NMe})_2:\text{CO}$ , by boiling with aqueous potassium nitrite. On reducing this oxime with hydriodic acid, it is converted into the corresponding amine, *dimethyl-uramil*,  $\text{NH}_2.\text{CH}:(\text{CO.NMe})_2:\text{CO}$ , a basic crystalline substance.

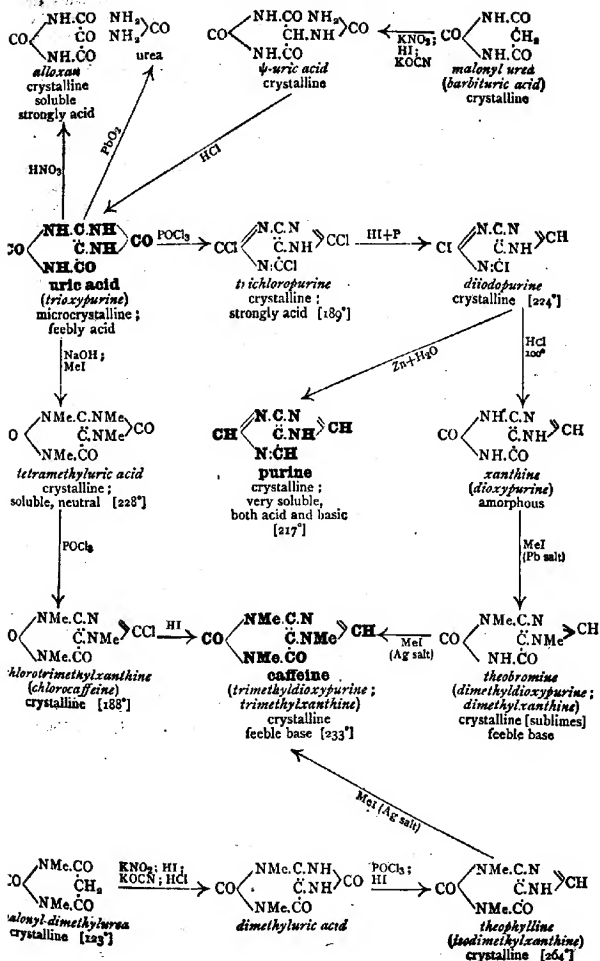
This amine is converted, by boiling with aqueous potassium cyanate, into the potassium salt of *dimethyl-ψ-uric acid*,  $\text{NH}_2.\text{CO.NH.CH}:(\text{CO.NMe})_2:\text{CO}$ , a crystalline substance which is readily dehydrated to *dimethyluric acid* by evaporation with hydrochloric acid. The conversion of the amine into the ψ-uric (pseudo-uric) acid is parallel to that of ammonia into urea by cyanic acid, and is an interaction of general applicability; uric acid is made synthetically from malonic acid and urea itself by a similar process.



The dimethyluric acid is convertible into dimethylxanthine by a process which is closely parallel to the conversion of uric acid into xanthine. On heating the dimethyl-acid with phosphorus pentachloride and oxychloride, it is converted into *chloro-dimethylxanthine*, which is reducible by hydriodic acid to a dimethylxanthine, *theophylline*. Theophylline is isomeric with theobromine, and when its silver salt is heated with methyl iodide is similarly methylated to trimethyl-xanthine, which is identical with caffeine (Fischer, 1895).



**200. Synopsis.**—Uric acid or trioxypurine, an important constituent of mammalian urine, and the chief constituent of the urine of birds and reptiles, is a complex ureide or urea amide. Theobromine and caffeine, the active constituents of tea, coffee and cocoa, are alkylated dioxypurines, closely related to uric acid.

$\text{NH}_2\text{CO NH}_2$ 

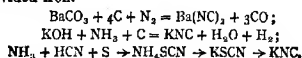


## CHAPTER XXXVI

### CYANOGEN COMPOUNDS : THE CYANIDES

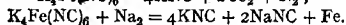
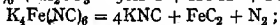
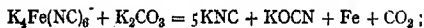
**201. The Simple and Double Metallic Cyanides.**—The metallic cyanides, which with prussic acid derive their name from Prussian blue (*καυρος*=blue), are substances of great technical importance, and are used in large quantities in gold extraction, electroplating, etc. They are manufactured to a certain extent by direct synthesis from the elements; the barium salt is thus produced when nitrogen is led over an intimate mixture of barium carbonate and carbon (pitch) heated at  $1400^{\circ}$ . They are chiefly obtained, however, as direct or indirect by-products of the manufacture of coal gas.

Besides ammonia, crude coal-gas contains a very appreciable amount of hydrogen cyanide, which is readily converted into Prussian blue by absorption with alkali containing ferrous and ferric hydroxides in suspension (§§ 54, 202). Fused potash containing carbon in suspension absorbs ammonia freely, forming pure potassium cyanide. Ammonium thiocyanate (§ 210) is made synthetically from ammonia and carbon disulphide, or by washing crude coal-gas (which contains both hydrogen cyanide and ammonia) with water in which sulphur is suspended; it yields pure hydrogen cyanide when distilled with dilute nitric acid, or calcium thiocyanate when heated with lime; the hydrogen cyanide is directly converted into the potassium salt, and the calcium thiocyanate is converted first into potassium thiocyanate, and then into cyanide by heating this with finely divided iron.



Potassium cyanide is also formed by fusing potassium ferrocyanide (§ 202) either with potassium carbonate, when potassium cyanate (§ 207) is also produced, or alone, when the product is free from this impurity; it is best prepared from the ferrocyanide by fusing the dry salt with metallic sodium, in which case it contains sodium cyanide, as well as the potassium salt, but no cyanate.\*

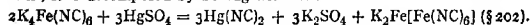
\* Commercial "98 per cent. gold cyanide" is usually such a product, and is both more economical and more efficient than the older product containing cyanate.



*Potassium cyanide*, K.N:C (Scheele, 1782), which was originally obtained by the interaction of potash and prussic acid, is a deliquescent, crystalline, exceedingly poisonous substance, which is readily soluble in water, but almost insoluble in absolute alcohol; owing to hydrolytic dissociation its solution is strongly alkaline, and smells of formonitrile. Solid potassium cyanide is quite stable in dry air, but when fused is readily oxidised, so that it is a powerful reducing agent.

The various metallic cyanides may be obtained from the potassium salt or from formonitrile. *Silver cyanide*, AgNC, is a white precipitate, which like silver chloride is soluble in ammonia, and reprecipitated by dilute nitric acid; but it is dissolved by this acid on prolonged boiling, and is not blackened by light.

*Mercuric cyanide*, Hg(NC)<sub>2</sub>, a colourless, sparingly soluble, crystalline salt resembling mercuric chloride, is formed by dissolving mercuric oxide in warm, dilute hydrocyanic acid, or by boiling mercuric sulphate with potassium ferrocyanide solution; its solution is not an electrolyte, and therefore does not react to the ordinary tests for mercury and cyanide ions; it is decomposed by boiling with zinc.



*Cuprous cyanide*, CuNC, is a white, insoluble substance resembling cuprous chloride, which is formed when copper sulphate is heated with an equivalent amount of potassium cyanide solution; the cupric cyanide which would be expected is immediately resolved into cuprous cyanide and free cyanogen (compare Cuprous iodide).



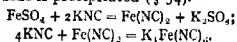
The cyanides of the heavier metals are mostly insoluble, but they nearly all combine with the alkali cyanides, forming soluble and more or less stable double salts. *Potassium argentocyanide*, KAg(NC)<sub>2</sub>, a soluble, crystalline salt which is used in electroplating, is formed by dissolving silver cyanide in potassium cyanide solution, and is reconverted into silver cyanide by dilute nitric acid.

*Potassium aurocyanide*, KAu(NC)<sub>2</sub>, is a similar compound. *Potassium cuprocyanide*, KCu(NC)<sub>2</sub>, is similarly formed from cuprous cyanide. Many such compounds are known; some of the metals, however, do not form these double salts—*lead cyanide*, Pb(NC)<sub>2</sub>, is insoluble in potassium cyanide solution.

**202. The Complex Metallic Cyanides.**—With metals of the iron group these compounds are much more stable, and must be termed **complex**, rather than double cyanides. The most

conspicuous is potassium ferrocyanide, which like the true double cyanides can be made by the direct union of the potassium and ferrous salts; when ferrous sulphate is warmed with excess of potassium cyanide solution, a clear yellow filtrate is obtained, which deposits potassium ferrocyanide crystals when evaporated (§ 54).

The ready synthesis of the alkali ferrocyanides provides the basis of the Prussian blue-test for nitrogen; when sodium is heated to bright redness with nitrogenous organic matter, sodium cyanide is formed with fair readiness; this interacts with the ferrous salt, forming the ferrocyanide, from which by addition of ferric chloride in acid solution ferric ferrocyanide or Prussian blue is precipitated (§ 54):



Potassium ferrocyanide was originally obtained by decomposing Prussian blue with caustic potash; it was afterwards prepared more directly by fusing horn, hoof-parings, and similar substances with potassium carbonate and scrap-iron, and until recently was manufactured in this way.

*Potassium ferrocyanide*,  $\text{K}_4\text{Fe}(\text{NC})_6 + 3\text{H}_2\text{O}$  (Macquer, 1750), forms large, transparent, yellow plates, which are tough and difficult to powder; it is not poisonous, nor does it give the ordinary reactions for iron or cyanide, the metallic and cyanogen ions being united in the complex quadrivalent ferrocyanogen ion,  $\text{Fe}(\text{NC})_6^{4-}$ .

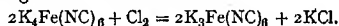
The corresponding acid, *hydroferrocyanic acid*,  $\text{H}_4\text{Fe}(\text{NC})_6$ , separates as a white precipitate on adding concentrated hydrochloric acid to a cold solution of the potassium salt.

*Prussian blue or ferric ferrocyanide*,  $\text{Fe}_4[\text{Fe}(\text{NC})_6]_3$  (Diesbach, 1704), which was originally obtained by the successive action of fused alkali and iron salts on nitrogenous organic matter such as dried blood, is a dark blue powder, which may be crystallised from cold, concentrated hydrochloric acid. When digested with caustic alkali it is converted into ferric hydroxide and the alkali ferrocyanide, from which it is at once reprecipitated by ferric salts in acid solution.

*Potassium ferrous ferrocyanide*,  $\text{K}_2\text{Fe}[\text{Fe}(\text{NC})_6]$ , and *copper ferrocyanide*,  $\text{Cu}_2[\text{Fe}(\text{NC})_6]$ , are the familiar light-blue (white) and reddish-brown precipitates obtained in testing for ferrous and cupric salts. *Silver ferrocyanide*,  $\text{Ag}_4\text{Fe}(\text{NC})_6$ , is a white insoluble precipitate; it interacts with ethyl iodide forming a crystalline ester, *ethyl ferrocyanide*,  $\text{Et}_4\text{Fe}(\text{NC})_6$ .

Unlike Prussian blue, potassium ferrocyanide is decomposed by acids, and when distilled with dilute sulphuric acid yields formonitrile. When the salt is heated with the concentrated acid, however, the formonitrile is at once resolved into carbon monoxide by successive hydrolysis and dehydration; potassium cyanide similarly yields carbon monoxide quantitatively when cold concentrated sulphuric acid is allowed to drop upon it.

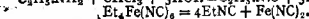
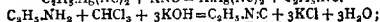
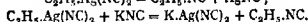
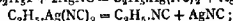
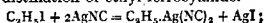
On oxidising potassium ferrocyanide by saturating its solution with chlorine or bromine it darkens in colour, and on concentrating the product the corresponding complex ferric cyanide crystallises out. *Potassium ferricyanide*,  $K_3Fe(NC)_6$  (Gmelin, 1822) crystallises in dark red prisms, and dissolves to a brownish solution; *ferrous erricyanide* or *Turnbull's blue*,  $Fe_3[Fe(NC)_6]_2$ , is a dark-blue precipitate, which resembles Prussian blue in appearance. *Ferric ferricyanide*,  $Fe[Fe(NC)_6]$ , which is probably identical with ferric cyanide, is soluble in water and greenish-brown in colour.



**203. The Alkyl Cyanides.**—Alkyl compounds, such as ethyl potassium sulphate and ethyl iodide, interact with potassium cyanide, forming compounds which have the composition of alkyl cyanides, and are identical with the acid nitriles (§§ 56, 64). The simplest nitrile, formonitrile (§ 61), is hydrogen cyanide. If, however, the potassium cyanide be replaced by the cyanide of a heavy metal, such as silver, isomeric compounds of an entirely different character are obtained.

When ethyl iodide is boiled in a reflux apparatus with dry silver cyanide it is rapidly absorbed, forming *ethyl argentocyanide*,  $EtAg(NC)_2$ , a soluble crystalline compound analogous to potassium argentocyanide; and on heating this salt, either alone at  $180^\circ$ , or with concentrated potassium cyanide solution at  $100^\circ$ , a liquid is obtained which is isomeric with propionitrile, and is termed ethyl isocyanide.

The same compound is formed when excess of caustic alkali is added to an alcoholic solution of chloroform and ethylamine hydrochloride, the action here being analogous to the formation of potassium cyanide from chloroform, ammonia and alcoholic potash. It is also produced in small quantities in the synthesis of nitriles by the alkyl-sulphate method, and is formed by simple distillation of ethyl ferrocyanide.



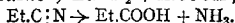
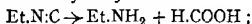
*Ethyl isocyanide* or *ethyl-carbylamine*,  $C_2H_5N:C$  (Gautier, 1865), is a volatile liquid boiling at  $78^\circ$ , which is characterised by a peculiarly offensive odour and taste, the vapour being nauseously bitter; but it is not as poisonous as propionitrile, which resembles formonitrile in its physiological action.

Unlike propionitrile, moreover, ethyl isocyanide is very stable towards alkalis, and can be dried with solid potash;

but it is hydrolysed by mineral acids with explosive violence, yielding formic acid and the salt of the corresponding amine, ethylamine. Like potassium cyanide, ethyl isocyanide dissolves silver cyanide with great avidity, forming a soluble argentocyanide, identical with that which is obtained in the course of its preparation.

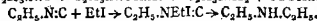
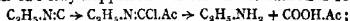
Many such isocyanides are known; they are all light, malodorous liquids, which are stable towards alkalis, are violently hydrolysed by acids; and form soluble, crystalline double salts with silver cyanide. When heated in a moist state at 200°, they are slowly transformed into the corresponding nitriles, of which they are thus the labile isomerides.

The formation of the isocyanides from chloroform and the amines, and their quantitative hydrolysis to the amines and formic acid show that the alkyl radical is linked to nitrogen; in the nitriles the alkyl is linked to a carbon atom, and is unconnected with the nitrogen, as this is eliminated as ammonia when the compound is hydrolysed.\*



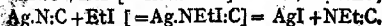
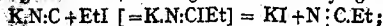
The cyanogen carbon of the carbylamines and metallic cyanides is bivalent or unsaturated, as in carbon monoxide; ethyl isocyanide combines additively with acetyl chloride, forming *pyroracemic ethylimino-chloride*,  $\text{CH}_3\text{CO.CCl:NEt}$ , which yields ethylamine and pyroracemic acid when hydrolysed, showing that the acetyl radical has united with the carbon of the isocyanide; many similar compounds have been prepared (Nef, 1892).

A further proof is afforded by the formation of secondary amines (§ 213), when the products which are formed by the interaction of the isocyanides and alkyl iodides, are hydrolysed; the union of the alkyl with nitrogen can only take place if the latter is trivalent (compare Amines, § 212), which can only happen in this case if the carbon is bivalent.

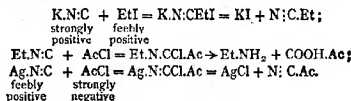


**204. Mechanism of the Cyanide Synthesis.**—The general analogy of the metallic cyanides to the alkyl isocyanides, their formation of soluble double silver salts, and the direct resolution of ethyl ferrocyanide into ethyl isocyanide and ferrous cyanide, leave no doubt as to their isocyanic constitution.

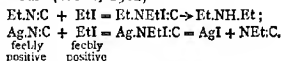
The formation of nitriles from the alkali (iso)cyanides, but of carbylamines from the (iso)cyanides of the heavy metals, is in all probability due to the intervention of unstable, intermediate additive compounds, the nature of which is dependent on the relative state of unsaturation of the (iso)cyanogen carbon and nitrogen under the varying conditions.



The carbon of potassium cyanide being bivalent and unsaturated, and the nitrogen trivalent and unsaturated, additive compounds analogous either to the acetyl chloride or the ethyl iodide compound of ethylisocyanide may be formed. When the metal is highly electropositive, as in potassium cyanide, the carbon is the more unsaturated, and nitriles are produced (Nef, 1892). The same occurs when the metal is relatively electropositive to the added radical, as in the combination of acetyl chloride with silver cyanide, when pyroracemic nitrile (acetyl cyanide) is formed; although silver is a feebly positive metal, it is strongly positive compared with the electronegative acetyl radical.



When, however, there is little electrochemical difference between the radical of the cyanide and that of the alkyl compound, as in the interaction of silver cyanide with the alkyl iodides, the nitrogen is the more unsaturated and isocyanides result (Wade, 1902).



**205. Formonitrile and the Metallic Cyanides.**—The properties of hydrogen cyanide coincide with those of the nitriles. It is rapidly hydrolysed by alkalis, whereas isocyanides are particularly stable towards these agents; like the nitriles it is only slowly decomposed by concentrated hydrochloric acid, and it does not dissolve silver cyanide to any appreciable extent. Its production by the dehydration of formamide (§ 61) and formaldoxime (§86) also indicates a nitrilic character, and its physical, as well as its physiological properties, agree with those of the nitriles, and differ from those of the isocyanides.

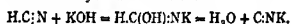
The metallic cyanides are in fact not salts of formonitrile, but of a labile isomeride, *hydrogen isocyanide* (Gautier, 1868), to which ordinary hydrogen cyanide bears the same relation as the nitriles to the isocyanides.

The interconvertibility is explained on the above electrochemical grounds. All acids necessarily contain electronegative radicals, and therefore combine with the carbon of the metallic cyanide, whatever the metal may be; and the additive compound breaks up into formonitrile and the metallic salt of the acid, just as the alkyl compounds form the homologous nitriles.



The reverse conversion of formonitrile into salts of isohydrocyanic acid is effected by a similar additive mechanism; the ions of the alkali combine with the nitrogen and carbon of the nitrilic cyanogen (compare Nitro-

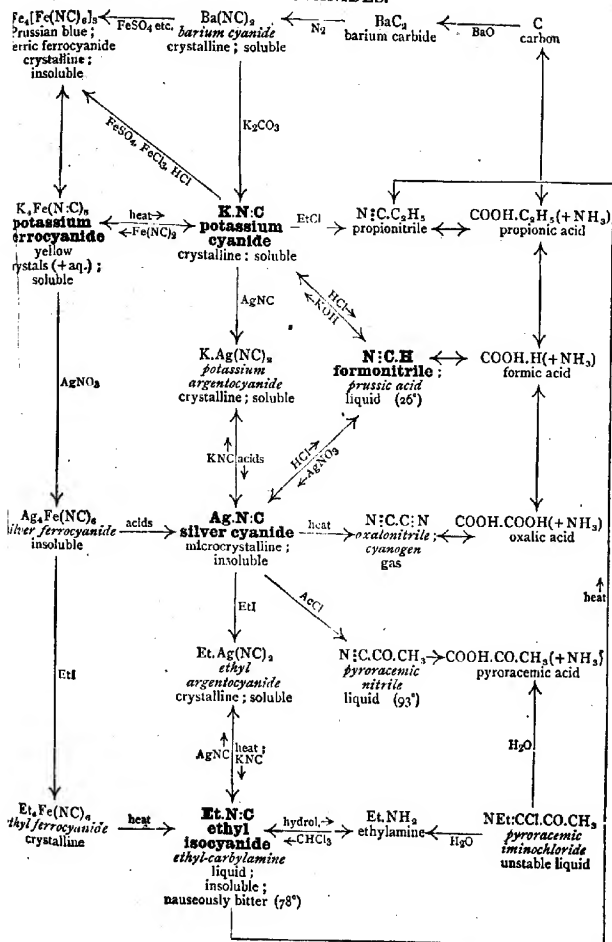
methane, § 232), forming additive compounds which are immediately resolved into the metallic cyanide and water.



The formation of both nitriles and isocyanides from metallic cyanides has also been explained by the assumption that hydrogen cyanide is a "tautomeric" compound, in the molecule of which the hydrogen atoms "wander" between the nitrogen and the carbon (compare § 144).

**206. Synopsis.**—The cyanogen radical resembles the halogens in forming metallic salts akin to the haloid salts in stability. On the other hand, the corresponding alkyl salts show the characteristic mobility of organic compounds. All the alkyl cyanogen compounds exist in two isomeric forms, in one of which, the iso-form, the alkyl is linked directly to nitrogen; the metallic cyanides correspond with the isocyanides, whilst hydrogen cyanide is a nitrile, the acid corresponding with the metallic (iso)cyanides being unknown.

## THE CYANIDES.

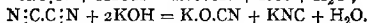
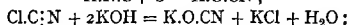
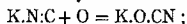




## CHAPTER XXXVII

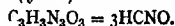
### CYANOGEN COMPOUNDS : THE CYANATES AND RELATED COMPOUNDS

**207. The Metallic and Alkylie Cyanates : Cyanic Acid.**—When fused potassium cyanide is exposed to air, or mixed with some easily reducible substance, such as red lead or manganese dioxide, it rapidly absorbs oxygen and is converted into potassium cyanate. The same compound is formed when cyanogen chloride vapour or cyanogen itself is led into caustic potash solution, the action being similar to the formation of hypochlorite from chlorine. It is also produced by the action of oxidising agents, such as potassium permanganate or sodium hypochlorite, on potassium cyanide solution.

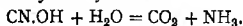


*Potassium cyanate*,  $\text{K.O.C:N}$  (Wöhler, 1824) is a crystalline substance resembling potassium chlorate ; it is freely soluble in water, but only sparingly so in alcohol ; the aqueous solution is unstable, and rapidly hydrolysed to ammonia and potassium carbonate. Potassium cyanate forms precipitates with most metallic solutions ; *lead*, *silver*, and *mercurous cyanates* are white, whilst *cuprous cyanate* is green ; silver cyanate is readily prepared in crystalline form by evaporating a solution of urea with silver nitrate in molecular proportion.

*Ammonium cyanate*,  $\text{NH}_4.\text{O.CN}$ , is a very unstable crystalline substance which is interconvertible with its isomeride, urea or carbamide ; it is formed by direct union of cyanic acid vapour with ammonia at a low temperature. Cyanic acid cannot be prepared from the potassium salt on account of the rapidity with which it is hydrolysed ; it is formed by distilling its polymeride, cyanuric acid (§ 208) in a current of carbon dioxide,

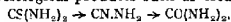


*Cyanic acid*,  $\text{CN.OH}$  (Wöhler, 1824), is a volatile acid liquid, resembling acetic acid in odour. It is very unstable, the pure liquid polymerising above  $0^\circ$ , with explosive violence, to a mixture of cyanuric acid, and another polymeride, *cyamelide*, which is a white substance resembling porcelain; its aqueous solution is also hydrolysed to carbon dioxide and ammonia at the same temperature, and potassium cyanate solution is therefore instantly hydrolysed by acids.



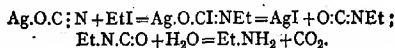
The chloride of cyanic acid is formed by the action of chlorine on mercuric cyanide or aqueous hydrocyanic acid. *Cyanogen chloride*,  $\text{CN.Cl}$ , is a pungent volatile liquid, which boils at  $15^\circ$ , and freezes at  $-5^\circ$ ; it is very poisonous. It is hydrolysed by alkalis in the normal manner to the alkali chloride and cyanate, and when its vapour is led into concentrated ammonia, it is converted, also normally, into the corresponding amide. Cyanamide is best prepared, however, by the action of mercuric oxide on thiocarbamide (§ 210).

*Cyanamide*,  $\text{CN.NH}_2$  (Clöez, 1851), is a hygroscopic crystalline substance, which melts at  $40^\circ$ , but soon polymerises at this temperature. As an ammonia derivative, it forms salts with the stronger acids, but owing to the influence of the electronegative cyanogen, its acid properties are the more prominent; on adding ammoniacal silver nitrate to an aqueous solution of the amide, yellow *silver cyanamide*,  $\text{CN}_2\text{Ag}_2$ , is precipitated. Cyanamide combines with water, forming carbamide, to which it is thus related in the same way as acetonitrile to acetamide; it has been used also in the synthesis of various physiological products such as creatine (§ 228).



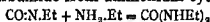
The labile or normal alkyl cyanates are unknown (see Cyanates, below), but the alkyl isocyanates or carbimides are formed in the same way as the isocyanides, and are hydrolysed in an analogous manner, although by alkalies, as well as by acids. Ethyl isocyanate is formed either by distilling a dry mixture of ethyl potassium sulphate and potassium cyanate, or by heating silver cyanate with ethyl iodide. The isocyanates are also transiently formed by the action of potash on the bromamides, during their conversion into amines (§ 212).

*Ethyl isocyanate* or *ethyl-carbimide*,  $\text{C}_2\text{H}_5\text{N:CO}$  (Wurtz, 1848), is a liquid which boils at  $60^\circ$ , and has a very pungent and unpleasant odour. It is hydrolysed by caustic soda to sodium carbonate and ethylamine, whence its constitution; ethylamine was first made as a result of this interaction.



When heated with water in a sealed tube, ethyl carbimide is converted into a substituted urea, *diethylcarbamide*,  $\text{CO}(\text{NHET})_2$ , the ethylamine

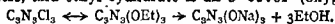
combining with a second molecule of the carbimide; the action is analogous to the synthesis of carbamide from ammonium cyanate.



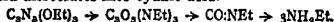
**208. The Cyanurates.**—When cyanogen chloride is dissolved in alcoholic sodium ethoxide, the ethyl cyanate which might be expected is not formed, ethyl iminocarbonate,  $\text{NH:C(OEt)}_2$  (§ 227) being produced. The polymeric cyanuric esters are known, however; they are prepared from cyanuric acid, a compound which is formed by heating urea (§ 193), and which also results, together with cyamelide, from the spontaneous polymerisation of cyanic acid.

*Cyanuric acid*,  $\text{CO} \begin{smallmatrix} \text{NH.CO} \\ \text{NH.CO} \end{smallmatrix} \text{NH}$  (Scheele, 1775) is a stable, crystalline, tribasic acid, which is resolved at a high temperature into cyanic acid, with which it can exist in equilibrium at an intermediate temperature. When treated with phosphorus pentachloride it is converted into cyanuric chloride,  $\text{C}_3\text{N}_3\text{Cl}_3$ , and would thus appear to be a hydroxy-compound (compare Uric Acid, § 197); but the presence of hydrogen in imido-form is proved by the conversion of the acid into a typical *nitrogen chloride*,  $\text{C}_3\text{O}_3(\text{NCl})_3$ , when its potassium salt is chlorinated (compare §§ 150, 252).

*Cyanuric chloride*,  $\text{CCl} \begin{smallmatrix} \text{N} = \text{CCl} \\ \text{N} - \text{CCl} \end{smallmatrix} \text{N}$ , a crystalline substance melting at  $146^\circ$ , is also formed by the spontaneous polymerisation of cyanogen chloride; it is hydrolysed to the alkali cyanurate by alkalis. When cyanuric chloride is warmed with alcoholic sodium ethoxide, or silver cyanurate is digested with ethyl iodide at the ordinary temperature, the ethyl ester of the acid is formed. *Ethyl cyanurate*,  $\text{C}_3\text{N}_3(\text{OEt})_3$ , is a crystalline substance which is hydrolysed by alkalis to alcohol and sodium cyanurate, and is converted into cyanuric chloride by phosphorus pentachloride. The alkyl groups are therefore linked to oxygen as in ordinary esters, and ethyl cyanurate is an *O*-ester (oxygen ester).



When, however, ethyl cyanurate is overheated, or silver cyanurate is heated with ethyl iodide, an isomeric ester is formed. *Ethyl isocyanurate*,  $\text{C}_3\text{O}_3(\text{NEt})_3$ , is a crystalline substance resembling the normal or labile cyanurate; but it is resolved by caustic soda into sodium carbonate and ethylamine, and does not yield cyanuric chloride with phosphorus pentachloride. The alkyl groups are therefore associated with the nitrogen atoms, and ethyl isocyanurate is an *N*-ester (nitrogen ester). When heated at  $500^\circ$ , ethyl isocyanurate dissociates into ethyl isocyanate, just as cyanuric acid dissociates into cyanic acid.

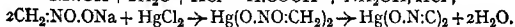
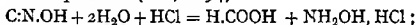


**209. The Fulminates.**—By the action of metallic mercury or silver on a mixture of alcohol and nitric acid, explosive metallic

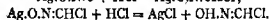
compounds are formed, termed fulminates, which are isomeric with the cyanates. The alcohol is cautiously poured into a large flask containing the mercury and moderately concentrated nitric acid, and the violent action which soon sets in is moderated by adding more spirit; on cooling the product after the action has ended, the metallic fulminate crystallises out.

*Mercuric fulminate*,  $\text{Hg}(\text{O.NC})_2$  (Howard, 1800), is a crystalline, highly explosive substance, which detonates when struck, and is used in percussion caps and dynamite fuses. *Silver fulminate*,  $\text{Ag.O.NC}$ , is a similar substance which is too unstable and dangerous to be of practical use. *Sodium fulminate*,  $\text{Na.O.NC}$ , a crystalline salt resembling sodium cyanide, is formed by the action of sodium amalgam on mercuric fulminate solution. *Fulminic acid* or *carbyloxime*,  $\text{HO.N:C}$ , is a very unstable poisonous substance, which is known only in solution.

The fulminates are quantitatively hydrolysed by warm hydrochloric acid to formic acid and hydroxylamine (Carstanjen, 1882), so that fulminic acid is the oxime of carbon monoxide, a view which is confirmed by the synthesis of mercuric fulminate from mercuric chloride and sodium isonitromethane (§ 232); mercuric isonitromethane is formed as an intermediate product (Nef, 1894).



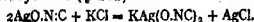
As an isocyanide (hydroxyisocyanogen) fulminic acid forms additive compounds in which the bivalent carbon becomes saturated. When silver fulminate is dissolved in the calculated amount of cold dilute hydrochloric acid, an additive compound, chloroformoxime, is formed, which can be extracted with ether from the product; part remains in solution as a silver salt.



*Chloroformoxime*,  $\text{H.CCl:N.OH}$  (Nef, 1894), is a pungent and very poisonous, crystalline substance, which is stable only in solution; the dilute solution smells like prussic acid, and was formerly mistaken for it. Chloroformoxime has acid properties; its *silver salt*,  $\text{H.CCl:N.OAg}$ , is stable in solution, although it contains both silver and chlorine, and gives precipitates with both silver nitrate and hydrochloric acid.

Sodium fulminate dissolves ferrous hydroxide in presence of caustic soda, forming *sodium ferrofulminate*,  $\text{Na}_4\text{Fe}(\text{O.NC})_6 + 18\text{H}_2\text{O}$ , a yellow crystalline salt, which closely resembles the alkali ferrocyanides, although less stable; it forms a characteristic purple-red coloration with ferric chloride, but is reconverted into silver fulminate by silver nitrate. Similarly silver fulminate is converted by potassium chloride into *potassium argento-*

*fulminate*,  $\text{KAg}(\text{O.NC})_2$ , a soluble crystalline salt resembling the corresponding argentocyanide (§ 201).



**210. The Thiocyanates and Thiocarbimides.**—Potassium cyanide combines with sulphur as readily as with oxygen, forming potassium thiocyanate or sulphocyanide. The salt may be prepared either by boiling potassium cyanide solution with sulphur, or fusing potassium ferrocyanide with potassium carbonate and this element; in the latter case it is extracted from the cooled melt with hot alcohol.

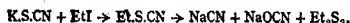
The corresponding ammonium salt is made by the action of alcoholic ammonia on carbon bisulphide; the mixture is kept for a day or two in the cold, and, on distilling the product, ammonium sulphide passes over, whilst an impure alcoholic solution of the thiocyanate remains. Ammonium thiocyanate is also formed when hydrocyanic acid is evaporated to dryness with yellow ammonium sulphide, or in a similar manner from crude coal-gas.



*Potassium thiocyanate*,  $\text{K.S.C:N}$  (Porret, 1814), is a deliquescent salt, which is extremely soluble in water; *ammonium thiocyanate* is very similar; *ferric thiocyanate* dissolves to an intensely red solution in water, and hence serves as a delicate test both for ferric iron and for hydrocyanic acid; *mercuric thiocyanate* is an amorphous, grey precipitate, which swells up curiously when burned. The free acid is obtained by distilling either salt with dilute sulphuric acid; *thiocyanic acid* is a volatile, pungent liquid which changes at once into a solid polymeride on warming; it is hydrolysed to ammonia and carbon oxysulphide by more concentrated acid.

When ammonium thiocyanate is heated for some time at  $170^\circ$ , it is transformed into thiocarbamide, in the same way as ammonium cyanate is changed into carbamide, and as with the cyanate the action is reversible. *Thiocarbamide* or *thiourea*,  $\text{CS}(\text{NH}_2)_2$  (Reynolds, 1869), is a silky, crystalline substance, which melts at  $169^\circ$ , and resembles urea in its actions; like cyanamide, into which it is readily converted by desulphurisation with mercuric oxide, it forms two classes of alkyl derivatives.

The labile or normal thiocyanates are formed by the interaction of the alkyl iodides with the alkali thiocyanates. *Ethyl thiocyanate*,  $\text{C}_2\text{H}_5\text{.S.CN}$ , is a liquid which boils at  $141^\circ$ , and resembles onions in odour; it is hydrolysed by caustic soda to sodium cyanide and cyanate, and an alkyl sulphur derivative, ethyl disulphide, so that the ethyl radical is attached to the sulphur alone and not to the cyanogen. When overheated the normal alkyl thiocyanates are transformed into the more stable mustard oils.



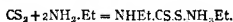
The stable isothiocyanates or mustard oils are made from carbon bisulphide and the primary amines, and in some cases

are formed by heating the normal thiocyanates; some of them are natural products. Black mustard seed contains a glucoside, *potassium myronate*,  $C_{10}H_{18}KO_{10}NS_2$ , which is hydrolysed by an accompanying enzyme, *myrosin*, to glucose, potassium hydrogen sulphate, and allyl isothiocyanate, or oil of mustard; this oil can be distilled with steam from the product obtained by digesting the ground seed with water; it is identical with the product obtained by heating allyl thiocyanate.

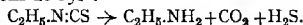
In synthesising the isothiocyanates, carbon disulphide and the amine, such as ethylamine, are dissolved in alcohol; the mixture becomes hot, and at the same time loses its alkaline reaction, and on cooling crystallises to the alkyl dithiocarbamate. On boiling the dithiocarbamate with mercuric chloride solution, the mercuric salt at first precipitated is decomposed into mercuric and hydrogen sulphides, and the isothiocyanate; the latter is distilled off with steam.



*Ethylamine ethyl-dithiocarbamate*,  $CS \begin{smallmatrix} NH_4Et \\ \diagup \\ S.NH_3Et \end{smallmatrix}$ , is a crystalline substance analogous to ammonium carbamate; the mode of its formation is precisely parallel in fact to that of this salt from ammonia and carbon dioxide.



*Ethyl isothiocyanate* or *ethyl-thiocarbimide*,  $C_2H_5.N:CS$  (Hofmann, 1868), is a liquid which boils at  $131^\circ$ , and has the intensely pungent and characteristic odour of mustard; it is hydrolysed by acids to ethylamine and carbon oxysulphide, or the products of hydrolysis of the latter, and the ethyl group is therefore linked to nitrogen. *Allyl isothiocyanate*,  $CH_2:CH.CH_2.N:CS$ , boils at  $151^\circ$ .



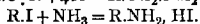
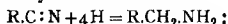
**211. Synopsis.**—The cyanates are derived from hydroxycyanogen, and yield carbonic acid and ammonia when hydrolysed; the thiocyanates are their sulphur analogues. The cyanic esters exist only in the stable form, in which the alkyl is linked to nitrogen, but both forms of the thiocyanic esters are known. The fulminates are derived from hydroxyisocyanogen, and yield formic acid and hydroxylamine when hydrolysed. The cyanurates are polymeric with the cyanates and form two series of esters, in which the alkyl is linked to nitrogen and oxygen respectively.



## CHAPTER XXXVIII

### THE AMINES AND AMMONIUM DERIVATIVES

**212. The Primary Amines.**—The amines homologous with methylamine and ethylamine are termed *primary amines*, as they bear the same relation to ammonia as the primary alcohols to water. Whilst methylamine and ethylamine may be prepared by reducing the corresponding nitriles, or by heating the alkyl iodides with alcoholic ammonia (§§ 57, 58), these processes are not of much use practically. The nitriles are difficult to prepare in quantity, and the primary amines formed by the ammonia process are accompanied by others, the separation of which is very tedious (§ 213). Both processes are general, however, in the sense that any primary amine can be made by means of them.



Various modifications have been devised in order to remedy this practical defect. Alkyl chlorides, bromides or nitrates (§ 230), or potassium alkylsulphates, may be substituted for the alkyl iodide, or the ammonia itself may be replaced by potassium phthalimide (§ 324), the alkyl derivatives of which yield pure primary amines when hydrolysed. Other alkyl-nitrogen compounds, such as the nitroparaffins (§ 231), aldehyde-ammonias, aldoximes and aldehyde-phenylhydrazones (§ 85) also yield primary amines when reduced. Pure primary amines are also formed by the hydrolysis of alkyl isocyanides (§ 203) and isocyanates (§ 207), but these compounds are too difficult to work with to render the method desirable. The cyanate hydrolysis is of historical interest as the first amine, ethylamine, was discovered accidentally in the course of decomposing ethyl isocyanate with caustic potash (Wurtz, 1848).

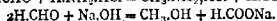
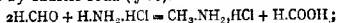
Practically, however, there is no general method by which aliphatic primary amines can be prepared in quantity, and special methods have to be used for the preparation of each particular amine. Methylamine is the most readily prepared of the aliphatic primary amines, as it can be made in quantity from acetamide and formaldehyde, both of which are readily accessible compounds.



When acetamide is treated with bromine at the ordinary temperature it is converted into *acetobromamide*, a colourless crystalline substance which forms a very unstable *potassium derivative*, when cold dilute potash is added to it. On adding the yellow solution thus obtained to warm concentrated potash, the potassium compound is decomposed into methylamine and carbon dioxide, owing to the intermediate formation of methyl isocyanate (Hofmann, 1881). The methylamine is accompanied only by a little ammonia, formed by a secondary action; it is purified by dissolving its hydrochloride in strong alcohol, in which ammonium chloride is only slightly soluble.



The formaldehyde method depends on a curious interaction between ammonium chloride and the aldehyde, which yield formic acid and fairly pure methylamine hydrochloride when heated together. The operation is carried out in concentrated aqueous solution at 60-100°, and a large excess of ammonium chloride is essential to the process; this, however, is recovered unchanged when the liquid product is concentrated on a water-bath, as it is insoluble in a concentrated solution of methylamine hydrochloride (Brochet, 1895). The action is akin to the decomposition of formaldehyde by caustic soda (§ 86).



The primary amines form a series which is graduated very similarly to the other homologous series. The lower members are very soluble, alkaline liquids, resembling methylamine and ethylamine (§ 57); their volatility and solubility alike decrease as the series is ascended, but even the highest amines have the same fundamental properties. The amines all form *additive salts* with acids, and these in turn form double salts such as the *platinichlorides* and *aurichlorides* (§ 59).

The primary amines are converted by nitrous acid into primary (or above ethylamine, secondary) alcohols; they form malodorous isocyanides (§ 203) by interaction with chloroform and alcoholic potash, and pungent mustard oils (§ 210) with carbon disulphide, etc. Finally, they interact with alkyl iodides even more readily than ammonia itself, forming secondary and tertiary amines (§ 213), and quaternary ammonium compounds (§ 214).

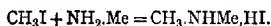
*Methylamine*,  $\text{CH}_3\text{NH}_2$  (Wurtz, 1849), resembles ammonia, and is one of the most soluble gases known, 1 cc. of water dissolving 1,150 cc. at 12°; like ethylamine it is inflammable, and condenses at -6° to a very light liquid which fumes strongly with acids; methylamine occurs naturally in the dog-mercury weed, and is formed as a bye-product from beet-sugar residues (§ 213).

*Ethylamine*,  $\text{C}_2\text{H}_5\text{NH}_2$  (§ 57), boils at 18°. *n-Propylamine*,

## 213. The Amines and Ammonium Derivatives 275

$\text{CH}_3\text{Et.NH}_2$ , boils at  $49^\circ$ , and *sec-propylamine*,  $\text{CHMe}_2.\text{NH}_2$ , at  $32^\circ$ . *n-Hexylamine*,  $\text{CH}_3.[\text{CH}_2]_4.\text{CH}_2.\text{NH}_2$ , is a light insoluble liquid boiling at  $128^\circ$ . *Cetylamine* or *hexadecylamine*,  $\text{CH}_3.[\text{CH}_2]_{14}.\text{CH}_2.\text{NH}_2$ , is a crystalline solid which melts at  $46^\circ$ , and has the essential properties of an amine.

**213. The Secondary and Tertiary Amines.**—The complex mixtures obtained by the prolonged interaction of alkyl iodides with ammonia contain compounds, which are related to the primary amines in the same way as these are to ammonia itself; methylamine interacts with methyl iodide precisely as ammonia does, forming a product, dimethylamine, the molecule of which is that of ammonia in which two hydrogen atoms are replaced by alkyl, and which is hence termed a secondary amine.



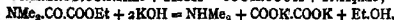
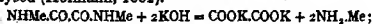
The dimethylamine in turn forms trimethylamine hydride, the salt of a tertiary amine; and finally the trimethylamine unites with the alkyl iodide additively, forming trimethylamine methiodide or tetramethylammonium iodide, a quaternary ammonium compound.



The product actually obtained by heating methyl iodide with alcoholic ammonia is therefore a mixture of all four salts with ammonium iodide, the primary and quaternary compounds predominating. On a large scale the alkyl bromides give better yields than the iodides.

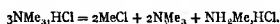
The separation of these amines is a matter of some difficulty, as the results of fractionation are unsatisfactory; it has been effected in the case of the lower amines by means of ethyl oxalate. The crude mixture of methylamines is distilled with caustic potash, by which the amine and ammonia salts are decomposed, whilst the tetramethylammonium iodide is unaffected.

The aqueous solution of the amines is then shaken with ethyl oxalate, which interacts with the amines in the same way as with ammonia, forming substituted oxamides or oxamic esters; the primary amine, methylamine, yields a crystalline substance, *symmetrical dimethyloxamide*,  $[\text{CO.NHMe}]_2$ , whilst the secondary amine is converted into an insoluble liquid, *ethyl dimethyloxamate*,  $\text{NMe}_2.\text{CO.CO.OEt}$ . The trimethylamine, which is unaffected, is then distilled off, and the two oxalic derivatives are separated and hydrolysed (Hofmann, 1862).



The secondary amines are difficult to prepare, and are usually made by special processes; dimethylamine is most conveniently obtained from *nitrosodimethylaniline* (§ 250), and even then the preparation is very

tedious. Dimethylamine occurs naturally with trimethylamine in fish, and can be obtained from herring-brine; trimethylamine is also present in hawthorn blossom. Trimethylamine is manufactured from "vinasses," the residual liquor from the distillation of beet-sugar alcohol; this is evaporated to dryness and distilled, yielding ammonia, trimethylamine, acetonitrile and methyl alcohol; the trimethylamine is converted into its hydrochloride, and again distilled, when it breaks up into methyl chloride, free trimethylamine and methylamine hydrochloride (Vincent, 1874). This amine is used in the preparation of potassium carbonate by the Solvay process, as its hydrochloride is much more soluble than potassium bicarbonate.



*Dimethylamine*,  $\text{NH}(\text{CH}_3)_2$  (Hofmann, 1851), is a heavy, soluble, alkaline vapour, which condenses at  $7^\circ$ , and resembles ammonia and stale fish in odour. *Trimethylamine*,  $\text{N}(\text{CH}_3)_3$ , is a similar vapour, which condenses at  $3^\circ$ , and has a still more pronounced odour of fish. The corresponding methyl compounds are much less volatile. *Diethylamine*,  $\text{NH}(\text{C}_2\text{H}_5)_2$ , boils at  $56^\circ$ , and *triethylamine*,  $\text{N}(\text{C}_2\text{H}_5)_3$ , at  $90^\circ$ .

Dimethylamine and trimethylamine differ from methylamine in that they do not form isocyanides with chloroform, mustard oils with carbon disulphide, or alcohols with nitrous acid. The latter agent has no action on the trialkyl-compounds, but it converts the secondary amines into nitroso-derivatives; *dimethylnitrosamine*,  $\text{NMe}_2\cdot\text{NO}$ , is an insoluble yellow oil, boiling at  $153^\circ$ .

As the nitrosamines are hydrolysed by concentrated hydrochloric acid, they are utilised for the separation of secondary from tertiary amines; excess of potassium nitrite is added to the solution of the mixed hydrochlorides, and the nitrosamine is extracted with ether and hydrolysed; the tertiary amine is then set free from the residue.



The isomerism of the amines is analogous to that of the ethers and alcohols. There are four compounds of the formula  $\text{C}_2\text{H}_5\text{N}$ ; two primary amines, propylamine and isopropylamine,  $\text{C}_3\text{H}_7\text{NH}_2$ ; one secondary amine, methyl-ethylamine,  $\text{CH}_3\text{NH}\cdot\text{C}_2\text{H}_5$ ; and one tertiary amine, trimethylamine,  $\text{N}(\text{CH}_3)_3$ .

Mixed amines are formed by the interaction of the simple amines with alkyl iodides; *methyl-ethylamine*,  $\text{CH}_3\text{NH}\cdot\text{C}_2\text{H}_5$ , an ammoniacal liquid which boils at  $35^\circ$ , and forms an oily nitroso-compound with nitrous acid, is made from methylamine and ethyl iodide or ethylamine and methyl iodide.



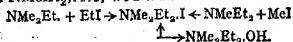
**214. The Quaternary Ammonium Compounds: Stereoisomerism of Nitrogen Compounds.**—The quaternary ammonium iodide, which remains when the final product of the interaction of ammonia and methyl iodide is distilled with potash, may also be made by the direct combination of trimethylamine with the alkyl iodide; it is readily crystallised from water, in which it is only sparingly soluble.

The rate of combination varies with the temperature, and also with the solvent (Menschutkin, 1895), the combination proceeding in methyl alcohol which is an ionising medium, nearly 300 times as fast as in hexane, which does not allow of the formation of ions.

*Tetramethylammonium iodide*,  $\text{NMe}_4\text{I}$  (Hofmann, 1851), is a crystalline substance which resembles potassium iodide, except that it is sparingly soluble; and it gives the ordinary reactions of an alkali iodide. It is not affected by caustic alkalies, but when its aqueous solution is warmed with excess of silver oxide, it becomes strongly alkaline, and the oxide is converted into yellow silver iodide. The alkaline solution has all the essential properties of caustic potash, and when evaporated under diminished pressure leaves a caustic, alkaline, translucent residue.

*Tetramethylammonium hydroxide*,  $\text{NMe}_4\text{OH}$  (Hofmann, 1862) is a crystalline, deliquescent, caustic substance, which, like potash, is highly alkaline and slippery to the touch. It forms salts with even greater energy, and rapidly absorbs carbon dioxide, forming a stable carbonate. It precipitates metallic hydroxides from their solutions, saponifies fats, and even liberates potash from potassium salts.

When the dry hydroxide is distilled, it is resolved into trimethylamine and methyl alcohol; but it is not a molecular compound of these substances, for it forms salts with elimination of water, and not by addition. Moreover, *dimethyl-diethyl-ammonium iodide*,  $\text{NMe}_2\text{Et}_2\text{I}$ , is formed equally well from dimethyl-ethyl-amine and ethyl iodide, as from methyl-diethyl-amine and methyl iodide, whereas if the ammonium iodide and hydroxide were molecular compounds, two different substances, of the formulae  $\text{NMe}_2\text{Et}, \text{EtI}$  and  $\text{NMeEt}_2, \text{MeI}$ , would be formed.



When the nitrogen atom of the quaternary ammonium compound is combined with four different alkyl groups, and the molecule thus rendered asymmetrical, the ammonium salt is resolvable into optically active, enantiomorphous isomerides.

*Methyl-ethyl-propyl-isobutyl-ammonium chloride*,  $\text{NMeEtPrBu}^{\text{B}}\text{Cl}$ , becomes *lævo*-rotatory when mould is allowed to grow on its solution (Le Bel, 1890), just as racemic acid does under the same conditions; and as there is no asymmetrical carbon in the molecule, the optical activity must be attributed to the asymmetry of the molecule with regard to the nitrogen atom.

Such opposite isomerides have been isolated by means of a strongly dextro-rotatory acid, *d*-camphorsulphonic acid (§ 341); this is a powerful acid, which forms dextro- and *lævo*-“ammonium” salts, differing from one another in the same way as strychnine *d*-lactate from strychnine *l*-lactate (§ 139). In both cases the salts differ in optical activity and are no longer enantiomorphous, and by reason therefore of their different solubilities they can be separated by fractional crystallisation (Pope, 1899).

*i*-*Methyl-allyl-phenyl-benzyl-ammonium iodide*,  $\text{NMe}(\text{C}_3\text{H}_5)(\text{C}_6\text{H}_5)(\text{C}_7\text{H}_7)\text{I}$  (Wedekind, 1899), a crystalline substance resembling tetramethylammonium iodide, is formed by the union of allyl iodide with methyl-phenylbenzylamine,  $\text{NMe}(\text{C}_6\text{H}_5)(\text{C}_7\text{H}_7)$ , a tertiary amine which is made by the action of benzyl chloride on methylaniline (§ 250).

When a solution of this quaternary iodide in acetone and ethyl acetate is boiled with silver *d*-camphor-sulphonate, it is converted into a mixture of the dextro-ammonium dextrosulphonate, and the *lævo*-ammonium dextrosulphonate, which are separable by fractional crystallisation from acetone. On adding potassium iodide to the solutions of the respective salts, the sparingly soluble iodides are precipitated, just as tetramethylammonium iodide is precipitated from its hydræide by the same agent; these iodides are optically active antipodes.

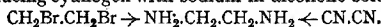
*d*-*Methyl-allyl-phenyl-benzyl-ammonium iodide* (Pope, 1899) is a crystalline substance resembling the tetramethyl-compound; it is markedly dextrogyrate  $[\alpha]_D = +52^\circ$ ; the corresponding *lævo*-compound is precisely similar in every respect, except that it is *lævog*gyrate,  $[\alpha]_D = -51^\circ$ .

Other elements such as sulphur and tin form similar asymmetrical derivatives, which have been proved to be similarly resolvable into optically active isomerides. Optical activity is thus not confined merely to compounds whose molecules contain asymmetrical carbon atoms, but rests on the broader basis of general intramolecular asymmetry (Pope, 1899 et seq.).

**215. The Diamines.**—Whilst the amines are best regarded as derivatives of ammonia, they are also substitution-products of the hydrocarbons; methylamine is *amino-methane*, and poly-amino-derivatives analogous to the glycols may therefore be expected. The chief of these are the diamines.

which are prepared by methods analogous to those employed in the preparation of the monamines.

Ethylene diamine, the analogue of glycol, is obtained by the action of alcoholic ammonia on ethylene bromide at  $100^{\circ}$ , or by reducing cyanogen with sodium in alcoholic solution.

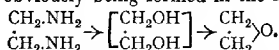


*Ethylene diamine* or *diamino-ethane*,  $\begin{array}{c} \text{CH}_2 \cdot \text{NH}_2 \\ | \\ \text{CH}_2 \cdot \text{NH}_2 \end{array}$  (Clôez, 1853),

is an alkaline liquid of ammoniacal odour, boiling at  $116^{\circ}$ ; it forms additive salts with acids in the same way as the monamines, but as the molecule contains two basic nitrogen atoms, twice as much acid is neutralised as by a molecular proportion of a monamine.

Similarly, the *dihydrochloride*,  $\text{C}_2\text{H}_4(\text{NH}_2)_2 \cdot 2\text{HCl}$ , is convertible into the *diplatinichloride*,  $\text{C}_2\text{H}_4(\text{NH}_2)_2 \cdot 2\text{HCl} \cdot \text{PtCl}_4$ , which contains only one molecule of the base per atom of platinum, instead of two, as with the monamines (§ 59); the number of basic nitrogen atoms is thus determined.

Ethylene diamine, like all amines, is not decomposed by alkalis or acids, and is converted by nitrous acid into ethylene oxide, glycol obviously being formed in the first instance.



The higher homologues of ethylene diamine are of importance on account of their identity with the *ptomaines* or *animal alkaloids*, which are formed by the putrefactive action of certain bacteria on albumen and related animal products (Selmi, 1884). The tetramethylene compound is formed by reducing ethylene cyanide with sodium amalgam in alcoholic solution, and the pentamethylene compound is made from trimethylene cyanide in a similar manner; *trimethylene cyanide* is made synthetically from the corresponding *bromide*, which is formed by heating allyl bromide with aqueous hydrobromic acid at  $150^{\circ}$ .

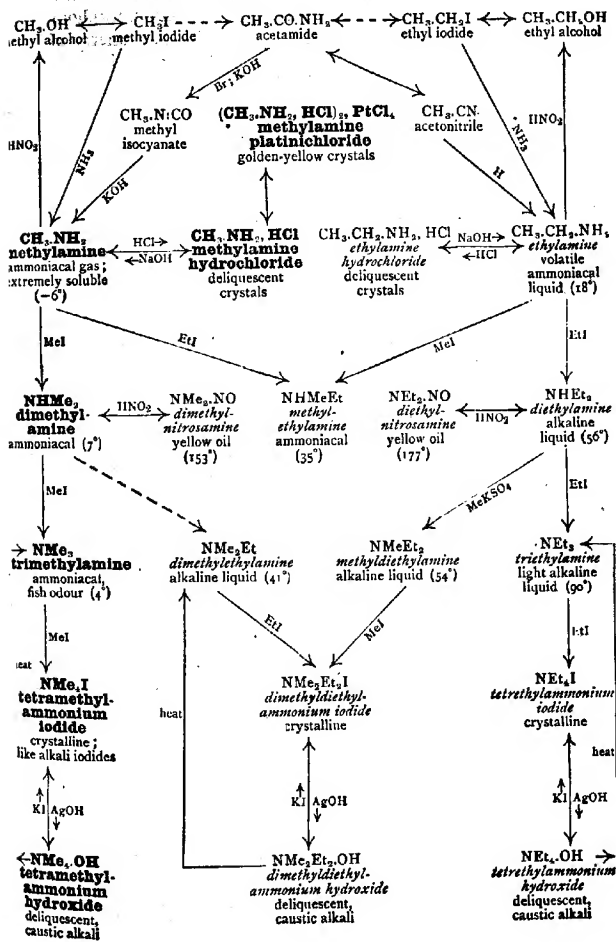
*Tetramethylene diamine* or *putrescine*,  $\begin{array}{c} \text{CH}_2 \cdot \text{CH}_2 \cdot \text{NH}_2 \\ | \\ \text{CH}_2 \cdot \text{CH}_2 \cdot \text{NH}_2 \end{array}$  (Ladenburg, 1886),

is a fuming alkaline liquid which boils at  $158^{\circ}$ , solidifies at  $24^{\circ}$ , and resembles piperidine in odour; it is a powerful base, and absorbs carbon dioxide freely. *Pentamethylene diamine* or *cadaverine*,  $\begin{array}{c} \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{NH}_2 \\ | \\ \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{NH}_2 \end{array}$  is a similar liquid, boiling at  $178^{\circ}$ ; it is readily convertible into piperidine (§ 388), an alkaloid obtained from pepper.

**216. Synopsis.**—The amines are derived from ammonia by replacing hydrogen by one or more alkyl groups, and from the hydrocarbons by similarly introducing one or more amino-groups. They are all highly basic substances, which form

ammonium salts with acids and alkyl iodides, and are not hydrolysed by alkalies; the asymmetrical quaternary compounds are resolvable into optically active enantiomorphous isomerides, the activity of which is due to the asymmetry of their molecules with regard to the nitrogen atom.

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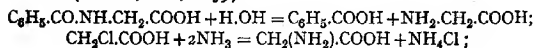




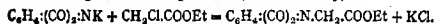
## CHAPTER XXXIX

### THE PRIMARY AMINO-ACIDS AND THEIR DERIVATIVES

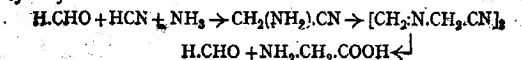
**217. Amino-Acetic Acid.**—Glycine or amino-acetic acid is a sweet substance which was originally obtained by hydrolysing glue or gelatine, and hence termed *glycocol* ( $\gamma\lambda\upsilon\kappa\upsilon\varsigma$ =sweet,  $\kappa\omicron\lambda\lambda\alpha$ =glue); it occurs naturally in the urine of herbivora in the form of a benzoyl compound, hippuric acid (§ 271), from which it may be prepared by hydrolysis with concentrated hydrochloric acid (Dessaigues, 1846). It may be made synthetically by heating chloracetic or bromacetic acid with a large excess of ammonia, but the yield is not good, as the corresponding secondary and tertiary amino-acids are also formed (Perkin, sen., 1859).



These bye-products may be avoided, however, by replacing the ammonia by phthalimide,  $\text{C}_6\text{H}_4(\text{CO})_2\cdot\text{NH}$  (§ 34). Potassium phthalimide interacts quantitatively with ethyl chloracetate, at  $150^\circ$ , forming *ethyl phthaloyl-glycine*,  $\text{C}_6\text{H}_4(\text{CO})_2\cdot\text{N}\cdot\text{CH}_2\cdot\text{COOEt}$ , a crystalline substance which is hydrolysed to phthalic acid, glycine and alcohol when heated with hydrochloric acid at  $200^\circ$ ; as the phthalimide molecule contains only one hydrogen atom linked to nitrogen, the formation of secondary and tertiary amino-compounds is impossible (Gabriel, 1889).

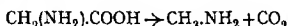


Glycine is readily prepared from formaldehyde by a modification of the cyanhydrin synthesis. Formaldehyde hydrocyanide condenses with ammonia, forming amino-acetonitrile, which condenses with more formaldehyde, forming a methylene compound; amino-acetic acid is readily made by the action of a large excess of aqueous ammonia on formaldehyde cyanhydrin.



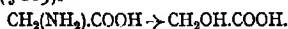
A cold concentrated solution of potassium cyanide is added slowly, with constant stirring, to a well-cooled solution of ammonium chloride in 40 per cent. formaldehyde, acetic acid being also added during the latter half of the process; the product eventually sets to a crystalline mass of an unstable compound, *methylene-aminoacetoneitrile* ( $\text{CH}_2\text{:N.CH}_2\text{.CN}$ )<sub>2</sub>. This substance, when hydrolysed by boiling with alcoholic hydrochloric acid, yields the hydrochloride of ethyl aminoacetate, whilst with aqueous hydrochloric acid free aminoacetic acid is formed (Curtius, 1894).

*Glycine or amino-acetic acid*,  $\text{CH}_2(\text{NH}_2)\text{.COOH}$  (Braconnot, 1821), is a sweet crystalline substance, which melts at  $232^\circ$ , and at the same time is partially decomposed into carbon dioxide and methylamine; the decomposition becomes quantitative when the substance is heated with solid baryta, and is parallel to that of acetic acid into methane and carbon dioxide. Glycine is fairly soluble in water, but almost insoluble in alcohol and ether.



Owing to the opposite actions of the amino-group and the carboxyl, glycine is almost a neutral substance; it is slightly acid to phenol-phthalein, but can only be titrated with alkali if the amino-group is protected by the addition of formaldehyde. Glycine is not appreciably decomposed by aqueous alkalis or acids, but like acetamide forms unstable salts both with acids, bases and alcohols, of which *glycine nitrate*,  $\text{C}_2\text{H}_5\text{NO}_2\text{.HNO}_3$ , the deep blue *copper salt*,  $\text{Cu}(\text{C}_2\text{H}_4\text{NO}_2)_2 + \text{H}_2\text{O}$ , and the deep-red *ferric salt*, may be mentioned. Like most complex amines glycine is readily oxidised, and reduces ammoniacal silver solutions (compare Aminophenols, § 294).

Glycine differs from acetamide in that being an amine, it is not hydrolysed by acids or alkalis; that it is a primary amine is proved by its conversion by nitrous acid into the corresponding hydroxy-compound, glycollic acid, which was first made in this way. When glycine ester is treated with nitrous acid, however, an intermediate product termed ethyl diazoacetate can be isolated, which undergoes some very interesting transformations (§ 219).



**218. Derivatives of Amino-Acetic Acid.**—As an acid, glycine forms esters, which are obtained as crystalline hydrochlorides when it is suspended in a solution of hydrogen chloride in the alcohol, and are also formed synthetically as above; the free esters are prepared by decomposing the hydrochlorides with concentrated aqueous potash at a low temperature; after

extraction with ether in presence of potassium carbonate they are fractionated under reduced pressure.

*Ethyl amino-acetate* or *glycine ester*,  $\text{CH}_2(\text{NH}_2).\text{COOEt}$  (Curtius, 1888), is a fragrant oil resembling cocoa in odour; it boils at  $35^\circ/15$  mm., or  $149^\circ/760$  mm.; its *hydrochloride* is a crystalline substance melting at  $144^\circ$ , and ~~its~~ *picrate*, which is a very characteristic salt, melts at  $157^\circ$ . Ethyl amino-acetate is strongly basic and fumes with acids, the amino-group no longer being counterbalanced by the carboxyl; it cannot be kept unchanged except when dissolved in dry ether.

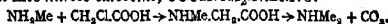
When glycine ester is evaporated with water it is converted into *glycine anhydride*,  $\text{CO} \langle \begin{smallmatrix} \text{CH}_2.\text{NH} \\ \text{NH}.\text{CH}_2 \end{smallmatrix} \rangle \text{CO}$ , a crystalline substance melting at  $275^\circ$ ; the action is parallel to the conversion of ethyl acetate into acetamide, and of lactic acid into lactide. Glycine anhydride is rapidly hydrolysed by boiling hydrochloric acid to *glycylglycine hydrochloride*, from which the free amino-acid is liberated by moist silver oxide. *Glycylglycine*,  $\text{NH}_2.\text{CH}_2.\text{CO}.\text{NH}.\text{CH}_2.\text{COOH}$ , is a sweet crystalline substance resembling glycine, and forms an *ester*, etc.; it is a dipeptide, the simplest member of the class of *polypeptides*, or synthetic products related to the *peptones* and more complex *proteins* (Fischer, 1901).

*Amino-acetonitrile*,  $\text{NH}_2.\text{CH}_2.\text{CN}$ , which is formed by the action of cold alcoholic ammonia on formaldehyde hydrocyanide, is an oily liquid boiling at  $58^\circ/15$  mm; like the ester it forms a crystalline *hydrochloride*, and it condenses with formaldehyde to the *methylene compound* described above. *Amino-acetaldehyde*,  $\text{NH}_2.\text{CH}_2.\text{CHO}$ , is a very unstable substance, obtained by hydrolysing the corresponding *acetal*,  $\text{NH}_2.\text{CH}_2.\text{CH}(\text{OEt})_2$ , which is formed by the action of ammonia on monochloroacetal,  $\text{CH}_2\text{Cl}.\text{CH}(\text{OEt})_2$  (§ 115).

By the interaction of chloroacetic acid with methylamine, a secondary amino-acid is formed, which bears the same relation to glycine as dimethylamine to methylamine.

*Sarcosine* or *methyl-glycine*,  $\text{NHMe}.\text{CH}_2.\text{COOH}$  (Liebig, 1847), is a crystalline substance, which melts and decomposes at  $220^\circ$ ; it occurs naturally in muscle fluid, and is formed by the hydrolysis of creatine (§ 228) and caffeine.

Like glycine it is neutral, and stable towards acids and alkalis, with which it forms similar salts—a deep-blue *copper* salt, a deep-red *ferrie* salt, etc. *Sarcosine ethyl ester*,  $\text{NHMe}.\text{CH}_2.\text{COOEt}$ , is an oily liquid boiling at  $43^\circ/10$  mm.; it is prepared in the same way as the glycine compound, and forms a similar crystalline *hydrochloride*. Sarcosine is decomposed by heat into carbon dioxide and dimethylamine; its constitution as a secondary amine is further confirmed by the action of nitrous acid, which converts it into *nitroso-sarcosine*,  $\text{COOH}.\text{CH}_2.\text{NMe}.\text{NO}$ .



**219. Ethyl Diazosuccinate: Diazomethane.**—Primary amines are invariably converted by nitrous acid into the corresponding alcohols, with evolution of

nitrogen, the action being due to the decomposition of amine nitrites, which are compounds resembling, but even more unstable than ammonium nitrite. With the amino-esters, however, these nitrites are sufficiently stable to be isolated, and to allow the process of decomposition to be followed; before undergoing complete decomposition they are converted into intermediate compounds, known as *diazo-esters*.

When ethyl amino-acetate hydrochloride, suspended in ether, is digested with silver nitrite, it is converted into *ethyl amino-acetate nitrite*,  $\text{COOEt} \cdot \text{CH}_2 \cdot \text{NH}_2 \cdot \text{HNO}_2$ , an insoluble substance which may be crystallised from alcohol; but if the alcoholic solution be heated to  $50^\circ$ , this nitrite is dehydrated to ethyl diazoacetate.

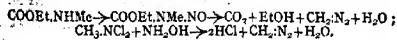
The same compound is formed directly by adding sodium nitrite to a concentrated aqueous solution of the ester hydrochloride; the product is extracted with ether, distilled with steam in presence of baryta, and dried with calcium chloride.

*Ethyl diazoacetate*,  $\text{CHN}_2 \cdot \text{COOEt}$  (Curtius, 1883), is a golden-yellow oil having a characteristic, penetrating odour; it is stable in presence of alkalis, but cannot be safely distilled, as it decomposes explosively when heated, forming nitrogen and ethyl fumarate. When mixed with water, ethyl diazoacetate is hydrolysed to ethyl glycolate and nitrogen; with alcohol it similarly yields ethyl ethoxyacetate, with concentrated hydrochloric acid it gives ethyl chloracetate, and with iodine it forms ethyl diiodacetate.

By means of this unstable intermediate compound, the number of types which can be prepared from amino-acids is greatly increased; owing to their instability very few aliphatic diazo-compounds have been isolated, but in the aromatic group they are much more stable and consequently more numerous (see Diazonium Compounds, § 258).

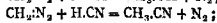
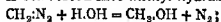
Most of the amino-esters form diazo-esters, which afford an excellent qualitative test for the presence of amino-acids. A small quantity of the substance is dissolved in absolute alcohol, and the solution is saturated with hydrogen chloride, the excess of which is then boiled off with the alcohol; the residual ester hydrochloride is now dissolved in a few drops of water covered with a little ether, and on the addition of a few crystals of sodium nitrite the diazo-compound is formed; it dissolves in the ether, and on evaporating the solvent in a watch-glass remains as a yellow, oily drop having a characteristic penetrating odour; on adding a drop of concentrated hydrochloric acid the ester dissolves, with effervescence, to a colourless solution of the corresponding chloro-acid.

The methane derivative corresponding with diazoacetic acid is made by the action of warm potash on *nitrosomethylurethane*,  $\text{NO} \cdot \text{NMe} \cdot \text{COOEt}$ , an irritating, corrosive, liquid, which is formed by passing nitrous fumes into an ethereal solution of *methyl-urethane*,  $\text{NHMe} \cdot \text{COOEt}$  (from methyl-isocyanate and alcohol at  $100^\circ$ ). Diazomethane is also produced by the interaction of hydroxylamine and *methyl-dichloramine*,  $\text{CH}_3 \cdot \text{NCl}_2$ , a volatile liquid which is formed by chlorinating methylamine hydrochloride with bleaching-powder.

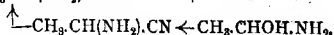
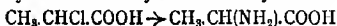


*Diazomethane*,  $\text{CH}_2 \cdot \text{N} \cdot \text{N}$  (Pechmann, 1894) is a yellow gas, which is readily condensed to a very volatile liquid; it is odourless, but very poisonous

and corrosive. Its actions are similar to those of ethyl diazoacetate, nitrogen being eliminated with most agents. It yields methyl alcohol with water, methyl chloride with hydrochloric acid, acetonitrile with hydrogen cyanide, and methylene iodide with iodine. When reduced with sodium and alcohol it is converted into *methyl-hydrazine*,  $\text{CH}_3\text{NH.NH}_2$ .



**220. Higher Amino-Acids.**—The chief of the fatty acid derivatives homologous with glycine are alanine and leucine. The first of these can be made synthetically from ammonia and  $\alpha$ -chloropropionic acid, and by the hydrolysis of aldehyde-ammonia cyanide with hydrochloric acid.



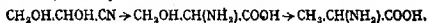
*Alanine* or  $\alpha$ -amino-propionic acid,  $\text{CH}_3\text{CH(NH}_2\text{).COOH}$  (Strecker, 1850), is a crystalline solid, which melts at  $255^\circ$ , and resembles glycine; it is decomposed when heated, quantitatively when heated with lime, into ethylamine and carbon dioxide. Alanine is indifferent to acids, but forms the usual coloured metallic salts and alkyl esters; *alanine ethyl ester* boils at  $48^\circ/11$  mm.; as a primary amine alanine is converted by nitrous acid into the corresponding hydroxy-compound, lactic acid, which was first synthesised in this manner.

As the alanine molecule contains an asymmetrical atom the substance should be resolvable into optically active antipodes; but as the acid and basic properties are so extremely feeble, the resolution cannot be effected in the ordinary manner. If however the alanine is converted into the *benzoyl alanine*,  $\text{CH}_3\text{CH(NHBz).COOH}$ , analogous to hippuric acid, by shaking with benzoyl chloride and sodium carbonate (§ 270), the acidity of the molecule is so much increased by the over-neutralisation of the amino-group that the benzoyl-acid forms stable salts with alkaloids.\*

In this way the benzoyl compound of synthetic alanine may be resolved by means of its *brucine salt* into *levo-benzoylalanine* and *dextrobenzoylalanine*, from which the corresponding *l-alanine* and *d-alanine* are liberated by hydrolysis; they both melt at  $207^\circ$ , and are equal and opposite in rotatory power (Fischer, 1899). Glycine cannot be decomposed in this manner, as its molecule does not contain an asymmetrical atom.

\* K glycine = 0.000,000,05; K hippuric acid = 0.0222.

$\beta$ -Hydroxyalanine or serine,  $\text{CH}_2\text{OH}.\text{CH}(\text{NH}_2).\text{COOH}$ , a crystalline substance melting at  $246^\circ$ , is the principal product of the hydrolysis of silk gelatine (§ 224); it is reduced to alanine when heated with hydriodic acid, and may be made synthetically in a similar manner to alanine, by hydrolysing the amino-derivative of glycollic aldehyde cyanhydrin (glyceronitrile) with hydrochloric acid.

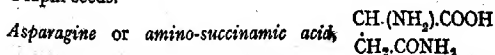


Cysteine or  $\alpha$ -aminothiolactic acid,  $\text{CH}_3.\text{C}(\text{SH})(\text{NH}_2).\text{COOH}$ , which is closely related to alanine, is a crystalline substance obtained by reducing cystine with tin and hydrochloric acid, and is readily reconverted into that substance by oxidation with air. Cystine,  $\text{S}_2[\text{CMe}(\text{NH}_2).\text{COOH}]_2$ , is the corresponding disulphide (§ 239); it is obtained by hydrolysis of albumen, casein, etc.

Leucine or  $\alpha$ -amino-isocaproic acid,  $\text{CHMe}_2.\text{CH}_2.\text{CH}(\text{NH}_2).\text{COOH}$  (Proüst, 1818), a crystalline substance, melting at  $170^\circ$ , is formed by hydrolysis of albumen and casein, and by boiling horn shavings with dilute sulphuric acid; it resembles its lower homologues in every respect, and can be made synthetically from  $\alpha$ -brom-isocaproic acid and from isovaleraldehyde. When boiled with manganese dioxide and dilute sulphuric acid it is oxidised to carbon dioxide and isovaleronitrile; its ethyl ester boils at  $83^\circ/12$  mm.

Synthetic leucine, as a racemic compound, is resolvable into its optical components in the same way as alanine, the cinchonine and quinidine salts of its benzoyl-compound being fractionated. The two benzoyl-compounds thus obtained melt at  $107^\circ$ , and are hydrolysed by 10 per cent. hydrochloric acid to *d*-leucine,  $[\alpha]_D = -17^\circ$ , and *l*-leucine,  $[\alpha]_D = +16^\circ$  (Fischer, 1899); the latter is identical with the product obtained from albumen, and may also be prepared by allowing mould to grow on the racemic compound (compare Racemic Acid, § 162). When *l*-leucine is heated with baryta-water at  $180^\circ$ , it is racemised, or converted into *d*-leucine, identical with the synthetic product.

**221. Dibasic Amino-Acids.**—Besides the monobasic amino-acids, there are amino-derivatives of the dibasic acids; the most important of these is amino-succinic or aspartic acid, a substance which occurs in beet-root, and is also obtained together with other amino-acids by hydrolysis of proteins (§ 222). The corresponding monamide, asparagine, is found in young beans and vetches, and especially in asparagus juice and lupin seeds.



(Vauquelin, 1805), is a sweet crystalline substance, like glycine; as an amide, it forms salts with bases and acids, and is hydrolysed by alkalis to the corresponding acid, amino-

succinic acid ; it may be prepared by heating ethyl bromo-succinate with strong ammonia at  $100^{\circ}$ . Both active modifications occur in nature, and may be obtained from the inactive or synthetic compound by the alkaloid method ; it is noteworthy that whilst the dextro-modification is sweet, the lævo-modification is tasteless (compare Selective Action of Enzymes, § 174).

Amino-succinic or aspartic acid,  $\text{CH}(\text{NH}_2)\text{COOH}$ , is a  
 $\text{CH}_2\text{COOH}$

crystalline substance resembling the other amino-acids ; the acid of beet is dextrogyrate, and is also formed by hydrolysis of albumen with alkali. As primary amines the aspartic acids are converted by nitrous acid into the corresponding hydroxy-compounds, the active malic acids.

Glutamic acid,  $\text{COOH}\cdot\text{CH}(\text{NH}_2)\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{COOH}$ , a crystalline substance resembling aspartic acid, is known chiefly as a product of protein hydrolysis. Lysine or *α*-diamino-caproic acid,  $\text{CH}_2(\text{NH}_2)\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}(\text{NH}_2)\cdot\text{COOH}$ , is similarly formed ; it is decomposed by putrefactive microbes into carbon dioxide and pentamethylene diamine,  $\text{CH}_2(\text{CH}_2\cdot\text{CH}_2\cdot\text{NH}_2)_2$  (§ 215), and has been made synthetically. Its next lower homologue, ornithine or diaminovaleric acid,  $\text{CH}_2(\text{NH}_2)\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}(\text{NH}_2)\cdot\text{COOH}$ , similarly yields tetramethylene-diamine ; the origin of these diamines in the putrefaction of tinned meats, etc., is therefore explained.

**222. The Proteins : Albumen and Derived Compounds.**—Excluding mineral matter and fat, the dry material of animal organisms consists of a complex assortment of nitrogenous compounds termed proteins, or proteids, which are ultimately resolvable into amino-acids. The proteins may be classified roughly into *typical proteins*, compound or *conjugated proteins*, and *albumenoids*. Of these, the conjugated proteins are combinations of albumens with other substances, such as *nucleic acid*, a derivative of purine, and need not be considered further.

The typical proteins are divided into the *albumens*, such as are present in blood-serum and white of egg, and the chemically very similar *globulins*, which differ from the albumens chiefly in being insoluble in water. The albumenoids, or substances which remain undissolved in the bones, skin, etc., comprise such substances as *keratin* or horn-material, and *collagen*, the glue-like basis of cartilage.

Certain vegetable globulins and animal albumens can be obtained in crystalline form. From the serum of the horse and from white of egg, crystalline albumens may be prepared by the following process. The viscid liquid is mixed with an

equal volume of a saturated solution of ammonium sulphate; the globulin fraction is filtered off, and the filtrate rendered distinctly acid with acetic acid; in the course of a few hours it becomes almost solid with soft, transparent, needle-shaped crystals, which may be drained in the usual way (Hopkins, 1898). The chemical individuality of the substance thus prepared is indicated by the constancy of its rotatory power after repeated fractional crystallisation.

*Egg-albumen* is a neutral crystalline substance, which is soluble in water and dilute solutions of alkalies and salts, from which it is precipitated unchanged by saturation with ammonium sulphate; it is lævo-rotatory, the rotatory power of recrystallised egg-albumen being  $[\alpha]_D = -31^\circ$ .

Albumen contains sulphur, as well as the elements of the constituent amino-acids; the analyses are not yet sufficiently concordant to justify a formula, but the molecular weight as determined by titration with alkali in presence of formaldehyde (compare Aminoacetic acid, § 217) is over 3000, whilst the cryoscopic method gives a still higher number.

When egg-albumen is heated at about  $73^\circ$ , it is coagulated, or rendered amorphous and insoluble; the same result is obtained by the action of strong alcohol or nitric acid, an excess of the latter of which causes also a brilliant yellow colour, from the formation of nitro-phenolic compounds (§ 294). Albumen forms a red coagulum when boiled with mercuric nitrate solution containing nitrous acid (Millon, 1837), and a delicate violet colour with caustic soda and very dilute copper sulphate, similar to that which is yielded by biuret under the same conditions. When albumen solution containing a little glyoxylic acid is brought into contact with concentrated sulphuric acid, as in the familiar ring test for nitric acid, an intense purple colour is developed by condensation of the glyoxylic acid with indole-amino-propionic acid (§ 407) formed by hydrolysis of the albumen; this forms a very delicate test (Hopkins, 1902).

Coagulated albumen cannot be redissolved in water, but like the simpler amino-acids it combines with dilute acids and alkalies, forming soluble acid albumens or *syntonins*, and alkali albumens or *albuminates*; these may be precipitated as insoluble salts by such agents as phosphomolybdic and phosphotungstic acids, copper sulphate and mercuric chloride.

On further treatment with hydrolytic agents the syntonins and albuminates are successively resolved into *albumoses* or non-coagulable albumens, and *peptones* or soluble proteins which can neither be coagulated nor salted out. The same transformation is effected during the process of digestion by the enzyme *pepsin* of the gastric juice (compare § 173).



The albumoses and peptones still give many of the characteristic colour reactions of albumen, but when further hydrolysed, preferably by heating with alcoholic hydrochloric acid, are resolved, in some cases quantitatively, into complex mixtures of amino-acids, which can be separated and identified, by means of their esters (Fischer, 1901).

The ester hydrochlorides, produced as a direct product of the hydrolysis, or prepared from the mixed amino-acids (compare Glycine ester, § 218), are converted into free esters, and these are separated by fractional distillation under low pressure, and identified by conversion into suitable crystalline derivatives such as the picrates, benzoyl-compounds, etc.

The chief amino-acid thus obtained from ordinary egg-albumen is *l*-leucine, of which the dry protein yields as much as one-fifth by weight; alanine, phenyl-alanine (§ 335), aspartic acid, cystine, and tyrosine (§ 335) also occur in considerable quantities; and glutamic acid, pyrrolidine-carboxylic acid (§ 407), serine, indole-aminopropionic acid (§ 407), arginine (§ 228) and glycine are formed in progressively decreasing amounts. Lysine and *histidine* (§ 408), which is probably a glyoxaline derivative, are also obtained under certain conditions.

*Casein* differs from the true albumens in containing phosphorus, probably in loose combination as phosphoric acid, and in being acid to litmus; it is only slightly soluble in water, and is not coagulable. The principal amino-acid obtained by hydrolysis of casein is *l*-leucine, of which as much as 30 per cent. by weight is formed; tyrosine and aspartic and glutamic acids are also produced in considerable quantities. When casein is hydrolysed by the enzyme *trypsin* of the pancreatic juice, it yields considerable quantities of indole-aminopropionic acid, cystine and tyrosine.

**223. Constitution of the Proteins: Synthetic Polypeptides.**—It is not yet definitely known how the amino-acid groups are combined in the molecule of albumen. The individual albumens are widely different chemically. Egg-albumen yields *aminohexoses* (16 per cent.) as well as the above amino-acids, whilst from serum albumen but a small quantity of these sugar derivatives (1 per cent.) is obtainable. Even in egg-white there are various non-crystallisable proteins whose general properties agree with those of the albumens.

Many complex polypeptides (§ 218), which resemble the peptones and higher proteins in giving the biuret reaction, and in some cases in being hydrolysed by trypsin, have been made synthetically; the more complex the product, the smoother is the synthesis, and the closer the resemblance.

Glycylglycine ester (§ 218) interacts with ethyl chlorocarbonate, forming *α*-carbethoxy-glycylglycine,  $\text{COOEt} \cdot \text{NH} \cdot \text{CH}_2 \cdot \text{CO} \cdot \text{NH} \cdot \text{CH}_2 \cdot \text{COOEt}$ ; a

crystalline substance melting at  $87^{\circ}$ , which is converted by liquefied ammonia at the ordinary temperature into the corresponding diamide. *a*-Carbamino-glycylglycinamide,  $\text{CONH}_2\cdot\text{NH}\cdot\text{CH}_2\cdot\text{CO}\cdot\text{NH}\cdot\text{CH}_2\cdot\text{CONH}_2$ , is a crystalline substance melting at  $270^{\circ}$ ; it gives a violet "biuret" colour with alkali and copper salts, and generally resembles the simpler proteins. The  $\text{—CO}\cdot\text{NH}\cdot\text{CH}_2\text{—}$  complex may be repeated almost indefinitely, and by this and analogous methods simple and mixed polypeptides (such as *glycylalanine*) have been synthesised, in which as many as five or six of these complexes may be present. Such compounds not only give the biuret reaction, and are precipitated by phosphotungstic acid, but are digested (*i.e.* hydrolysed) by trypsin.

Compounds of this type have also been prepared by cautious hydrolysis of proteins, and it is probable that the "biuret" reaction of proteins is due to the presence of the atomic complex  $\dot{\text{C}}\cdot\text{CO}\cdot\text{NH}\cdot\dot{\text{C}}$ .

The simplest natural complexes of amino-acids are the *protamines*, which are present in quantity in spermatic fluid. *Salmine*,  $\text{C}_{16}\text{H}_{31}\text{N}_9\text{O}_9$ , from salmon roe, is resolved by hydrolysis mainly into nucleic acid, arginine (over 80 per cent.), lysine and histidine; it gives the biuret reaction, and is hydrolysed by trypsin, gradually ceasing to give the biuret colour as the molecule is broken up. *Sturine*, from sturgeon roe, yields similar products. As arginine, lysine and histidine are also obtained under certain conditions by hydrolysis of albumens, it is probable that the proteins contain a protamine nucleus, associated with polypeptide groups, which yield the simple amino-acids, tyrosine, etc., when hydrolysed.

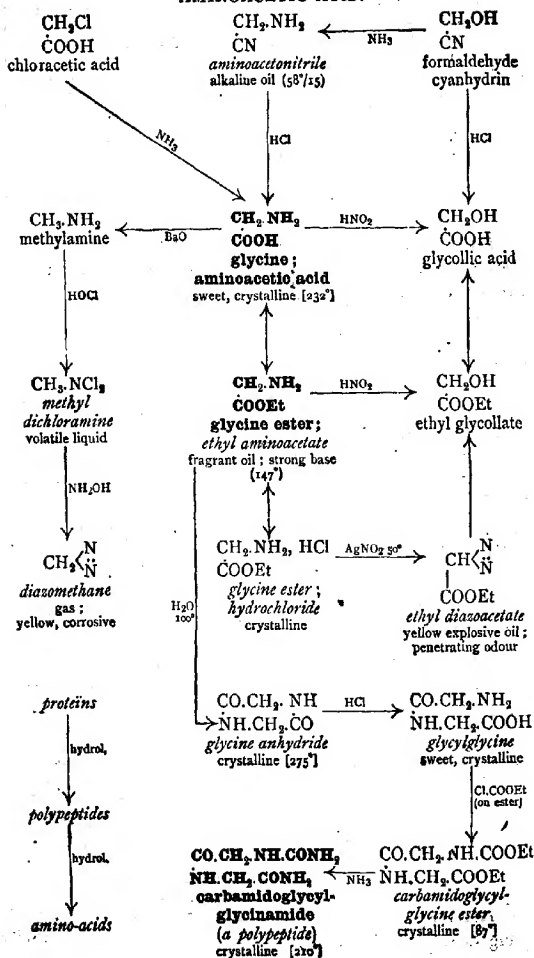
**224. The Proteins: Albuminoids.**—The chief of the albuminoids is *gelatine*, an amorphous substance which is soluble only in hot water, and is not coagulable by heat or nitric acid, although it is precipitated by mercuric chloride in acid solution and by tannin (§ 311). Gelatine has the essential characteristics of an amino-acid; its molecular weight, determined by titration with alkali in presence of formaldehyde, is over 4500.

The principal product of the hydrolysis of gelatine is glycine, of which it yields 16 per cent. by weight; the albumens do not yield much glycine. Pyrrolidine-carboxylic acid and leucine are also produced in large quantities, and glutamic acid, alanine, aspartic acid and phenylalanine are formed in smaller amounts; the optically active acids are to a large extent racemised at the high temperature required for the hydrolysis.

Silk is composed of *fibroin*, which forms the central portion of the fibre, and *sericin*, a glue-like substance which forms the outer coating. Sericin yields a large amount of serine when hydrolysed, whilst fibroin gives glycine (36 per cent.), *d*-alanine (21 per cent.), *l*-tyrosine (10 per cent.), with small quantities of *l*-leucine and *l*-phenylalanine.

**225. Synopsis.**—The amino-acids, the principal constituents of the proteins of nitrogenous animal compounds, are amino-substitution products of the carboxylic acids. They resemble the acid amides in their neutrality, but as amines they are not hydrolysable.

## AMINOACETIC ACID.



## CHAPTER XL

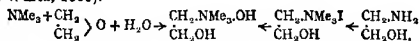
### COMPLEX AMINO-COMPOUNDS

#### 226. The Quaternary Amino-Acids and Related Compounds.—

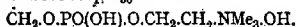
Several quaternary ammonium derivatives are known, which are closely related to glycine; the most important are the natural bases, choline, neurine and betaine. Choline is found in combination in bile, and in the brain and spinal cord; it occurs also in hops, and can be made synthetically.

*Choline* or *hydroxyethyl-trimethylammonium hydroxide*,  $\text{CH}_2\text{OH}.\text{CH}_2.\text{NMe}_3.\text{OH}$  (Strecker, 1862), is a deliquescent, difficultly crystallisable substance, which resembles tetramethylammonium hydroxide in character, and is a powerful base, absorbing carbon dioxide with avidity.

The constitution of choline is proved by two syntheses; the first, which establishes its relation to glycol, consists in the union of trimethylamine with ethylene oxide and water, and the second, which confirms its constitution as a quaternary ammonium compound, is effected by the successive action of methyl iodide and moist silver oxide on *hydroxyethylamine*,  $\text{CH}_2\text{OH}.\text{CH}_2.\text{NH}_2$ , a basic liquid formed by hydration of vinylamine (Baeyer, Wurtz, 1866).



*Lecithin*,  $\text{C}_{42}\text{H}_{86}\text{NPO}_4$ , an important constituent of brain matter, yolk of egg, etc., is a complicated fat or glyceride containing choline; it is a crystalline, wax-like substance, which dissolves only imperfectly in water. As it is hydrolysed by acids and alkalis to choline and glycerophosphoric and stearic acids, it is probably *choline distearyl-glycerophosphate*,

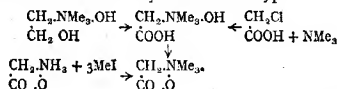


As a primary alcohol, choline is oxidisable to the corresponding acid, *hydroxy-trimethyl-aminoacetic acid*, the ammonium hydroxide corresponding with glycosine and sarcosine; the

anhydride of this acid is identical with betaine, the alkaloid of beet-root.

*Betaine* or *trimethyl-glycine*,  $\begin{array}{c} \text{CH}_2\text{NMe}_3 \\ \text{CO} \cdot \text{O} \end{array} + \text{H}_2\text{O}$  (Liebreich, 1869), is a sweet, deliquescent substance, which was first formed in the above manner. Unlike choline, it is neutral, the carboxyl forming a kind of internal ammonium salt with the ammonium group; it is broken up when heated with caustic alkali, the nitrogen being eliminated as trimethylamine.

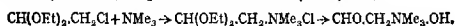
The constitution of betaine is confirmed by synthesis from chloracetic acid and trimethylamine, and from glycine and methyl iodide in presence of methyl alcohol and caustic alkali; and it is possible that glycine and sarcosine are also internal anhydrides of this type.



The corresponding aldehyde, *muscarine*,  $\begin{array}{c} \text{CH}_2\text{NMe}_3\text{OH} \\ \text{CHO} \end{array}$ , is

a very poisonous crystalline substance which is found in toad-stools.

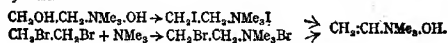
It may be prepared either by oxidising choline with nitric acid, or by hydrolysing the *acetal* which is formed synthetically from mono-chloroacetal and trimethylamine (compare Aminoacetaldehyde, § 218).



Although choline and betaine are innocuous, the corresponding ethylene derivative, neurine, is as poisonous as the aldehyde muscarine; it is noteworthy that very great physiological differences are produced by comparatively slight changes in atomic constitution. Neurine occurs in the brain, and is one of the ptomaines formed in the putrefaction of albumen; it can also be made synthetically.

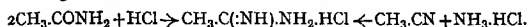
*Neurine* or *trimethyl-vinyl-ammonium hydroxide*,  $\text{CH}_2\text{CH} \cdot \text{NMe}_3\text{OH}$ , is a crystalline, powerfully basic substance.

It is made from choline by the successive action of hydriodic acid and moist silver oxide, and in a similar manner from ethylene bromide and trimethylamine.



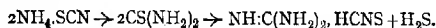
**227. The Amidines and Imino-ethers.**—When acetamide hydrochloride is heated in a sealed tube at 200°, it is partially converted into the hydrochloride of a base, acetamidine,

which may be regarded as acetamide, in which the oxygen is replaced by imidogen; the same compound is formed by heating acetonitrile with ammonium chloride.

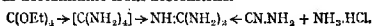


*Acetamidine*,  $\text{CH}_3\cdot\text{C}(\text{NH})\cdot\text{NH}_2$  (Strecker, 1857), is a highly alkaline liquid, which is easily hydrolysed to ammonia and acetic acid; it forms stable salts with acids, and even with nitrous acid, but does not yield a diazo-compound.

The corresponding carbonic acid derivative, carbamidine, bears the same relation to urea, and is identical with the guanidine obtained by oxidising guanine; it is best prepared by heating ammonium thiocyanate, the thiourea at first formed being resolved into guanidine thiocyanate and hydrogen sulphide.



Guanidine is also formed synthetically by the action of ammonia on ethyl orthocarbonate, the tetramino-derivative which might be expected breaking up into ammonia and the amidine; it is similarly produced by the direct union of cyanamide with ammonium chloride at  $100^\circ$ , in the same way as acetamidine from acetonitrile.

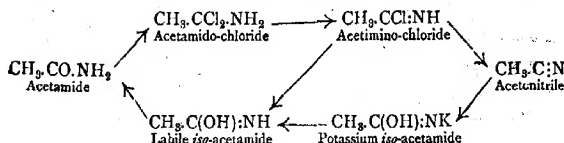


*Guanidine* or *carbamidine*,  $\text{NH}\cdot\text{C}(\text{NH}_2)_2$  (Strecker, 1861), is a very soluble, deliquescent, crystalline substance, which absorbs carbon dioxide freely, forming a crystalline carbonate; it is thus a powerful base. Like carbamide, it forms salts with one equivalent of acid only.

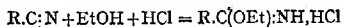
Guanidine is hydrolysed by baryta to ammonia and carbamide, and its constitution is confirmed by the above syntheses; when digested with a mixture of concentrated nitric and sulphuric acids, it is converted into nitroguanidine (below).

Acid amides are converted by phosphorus pentachloride into *amidochlorides*, very unstable substances, which readily lose hydrogen chloride and are converted into *imino-chlorides*. These also are unstable, and may be deprived of a second molecule of hydrogen chloride, yielding nitriles. Conversely the imino-chlorides are formed by the union of nitriles with hydrogen chloride.

These compounds are only definitely known in the aromatic group, but there is little doubt that the dehydration of amides by phosphorus pentachloride, and the hydrolysis of nitriles, are preceded by the formation of such imino-derivatives.

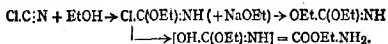


The esters of the iminochlorides are more stable substances, and can be prepared in the form of hydrochlorides by saturating alcoholic solutions of nitriles with hydrogen chloride.

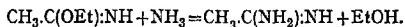


*Formimino-ether hydrochloride*,  $\text{H.C(OEt).NH.HCl}$ , is a crystalline, deliquescent substance, which is prepared in this way from hydrogen cyanide. *Acetimino-ether*,  $\text{CH}_3\text{C(OEt):NH}$ , is a somewhat unstable liquid, which boils at  $94^\circ$ , and has a characteristic odour; it is made by the action of potash on the hydrochloride.

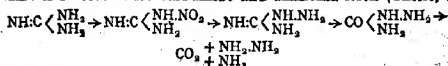
The analogous *ethyl iminocarbonate*,  $\text{NH.C(OEt)}_2$ , a light liquid boiling at  $140^\circ$ , is formed quantitatively by the action of alcoholic sodium ethoxide on cyanogen chloride at  $-10^\circ$ ; at higher temperatures, or in presence of water, urethane and ethyl cyanurate (§ 208) are also formed, probably by hydrolysis of the intermediate *chlorocarbimino-ether*,  $\text{Cl.C(OEt):NH}$ .



The imino-ethers are readily hydrolysed by the corresponding acids, with elimination of ammonia and alcohol; and they are converted into the corresponding amidines by ammonia, the action being analogous to the conversion of esters into amides.



When guanidine is digested with a mixture of concentrated nitric and sulphuric acids, it is converted into *nitroguanidine*,  $\text{NH.C(NH}_2\text{).NH.NO}_2$ , a crystalline substance melting at  $230^\circ$ , and on reducing this with zinc dust and acetic acid, it is converted into *amino-guanidine*,  $\text{NH.C(NH}_2\text{).NH.NH}_2$ , a highly basic substance. Amino-guanidine is stable in acid solution, but when set free by alkali it is successively converted into semicarbazide or amino-carbamide, and hydrazine or amino-ammonia, in the same way as guanidine is resolved into carbamide and ammonia itself (Thiele, 1893).



*Semicarbazide*,  $\text{NH}_2\text{CO.NH.NH}_2$ , a crystalline substance melting at  $96^\circ$ , is a useful reagent for aldehydes and ketones, with which it forms crystalline condensation-products, the *semicarbazones*. *Acetone-semi-*





creatine is convertible into the corresponding compound, creatinine, by heating with dilute acids, whilst the reverse transformation is effected by dilute alkalis.

*Creatinine*,  $\text{NH}_2\text{C} \begin{smallmatrix} \text{NMe.CH}_3 \\ \text{NH. CO} \end{smallmatrix}$  (Liebig, 1847), is a soluble crystalline substance, which forms well defined salts with acids, and liberates ammonia from ammonium salts. It is hydrolysed by baryta, not to sarcosine, but to *methyl-hydantoin*,  $\text{CO} \begin{smallmatrix} \text{NMe.CH}_3 \\ \text{NH. CO} \end{smallmatrix}$ , the methyl derivative of hydantoin or glycolyl urea; these complex amidines are therefore closely related to the natural ureides. When boiled with mercuric oxide and water, creatinine is hydrolytically oxidised to methylguanidine and oxalic acid.

**229. Synopsis.**—The quaternary ammonium compounds corresponding with glycine and sarcosine form internal anhydrides termed betaines, and are connected with quaternary amino-alcohols, aldehydes and ethylene derivatives, the latter of which are poisonous. The imino-ethers and amidines are esters and amides in which the carbonyl oxygen is replaced by an imino-group. The creatine of muscle is methylcarbamidine-acetic acid.

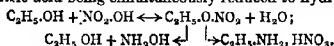
## CHAPTER XLI

### OXY-NITROGEN COMPOUNDS

**230. The Alkyl Nitrates and Nitrites.**—Practically all alcohols form nitrates of the type of the glycerol and cellulose compounds. The methyl and ethyl compounds are formed by digesting the alcohols with concentrated nitric acid, to which urea has been added to remove nitrous acid (the least trace of this compound sets up explosive oxidation of the alcohol); the nitrate is purified by washing with water, and after drying in the usual way is distilled.

The alkyl nitrates are heavy, insoluble liquids, having a pleasant odour. Like glycerol trinitrate, they are stable at ordinary temperatures, but when suddenly heated are liable to explode violently. *Methyl nitrate*,  $\text{CH}_3\text{O}\cdot\text{NO}_2$ , boils at  $65^\circ$ , and *ethyl nitrate*,  $\text{C}_2\text{H}_5\text{O}\cdot\text{NO}_2$  (Millon, 1843), at  $87^\circ$ . The constitution of these compounds is proved by their hydrolysis by caustic soda to the alcohol and sodium nitrate.

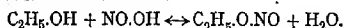
In their general actions they behave like the alkyl halogen compounds, and are thus converted into the corresponding amines by ammonia. When digested with tin and hydrochloric acid the alkyl nitrates are hydrolysed, the nitric acid being simultaneously reduced to hydroxylamine.



The corresponding nitrites are formed in a similar manner, either by passing nitrous gases into the alcohols, or by generating nitrous acid in contact with them.

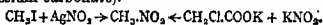
Ethyl nitrite is thus made by adding a mixture of alcohol and dilute sulphuric acid to sodium nitrite solution; the latter is placed in a tall cylinder, cooled in a freezing mixture, and the acid mixture, which is similarly cooled, is slowly added through a thistle-funnel-reaching to the bottom; the product eventually becomes semi-solid with sodium sulphate, whilst the insoluble ester rises to the surface; it is washed with water and dried with potassium carbonate. Amyl nitrite is similarly prepared by adding ice-cold concentrated sulphuric acid drop by drop, with constant stirring, to ice-cold amyl alcohol in which powdered sodium nitrite is suspended; the ester rises to the surface on diluting the product with water.

The alkyl nitrites are light, volatile, insoluble liquids, having a powerful, oppressive odour; like the nitrates, they are liable to explode when heated. *Methyl nitrite*,  $\text{CH}_3\text{O.NO}$ , boils at  $-12^\circ$ , and is gaseous at ordinary temperatures. *Ethyl nitrite*,  $\text{C}_2\text{H}_5\text{O.NO}$ , boils at  $17^\circ$ , and when dilute resembles apples in odour; the crude product obtained by distilling alcohol with copper, nitre, and sulphuric acid (Kunkel, 1681), is used in medicine under the name of sweet spirit of nitre. *Amyl nitrite*,  $\text{C}_5\text{H}_{11}\text{O.NO}$ , boils at  $96^\circ$ . The constitution of the nitrites is proved by their hydrolysis by alkalis to the alcohol and alkali nitrite.



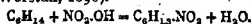
**231. The Nitro-Paraffins.**—The higher alkyl iodides are converted into nitrites when heated with silver nitrite, but the lower iodides yield isomeric compounds, the nitro-paraffins. When ethyl iodide is heated in a reflux apparatus with dry silver nitrite, the product is not homogeneous, and on fractionation is resolved into about equal parts of ethyl nitrite, boiling at  $17^\circ$ , and the isomeric nitroethane boiling at  $114^\circ$ . With methyl iodide the nitro-compound is the exclusive product.

The iodide is poured slowly down the condenser of a reflux apparatus containing the well-dried silver salt, and after the violent action has subsided the product is distilled from an oil-bath, and repeatedly redistilled over silver nitrite to remove the last traces of iodide. Nitro-methane is also conveniently obtained by boiling potassium chloracetate or bromacetate with concentrated potassium nitrite solution, the transiently-formed *nitro-acetate* (§ 233) decomposing into the nitro-paraffin and carbon dioxide (potassium carbonate).



The higher nitro-compounds are prepared by nitrating the corresponding paraffins. When *n*-hexane is heated with dilute nitric acid in a sealed tube at  $140^\circ$ , it is converted into  $\beta$ -nitrohexane; *n*-heptane and *n*-octane also yield similar products (Kononoff, 1894). The iso-paraffins are easily nitrated by digestion with concentrated nitric and sulphuric acids (compare Nitrobenzene, § 246).

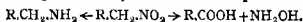
The normal paraffins are much less readily affected by this powerful nitrating agent; *n*-hexane, however, after boiling for some days, is converted into  $\alpha$ -nitrohexane, and *n*-heptane yields a similar product somewhat more easily (Worstall, 1898).



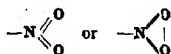
The nitro-paraffins are heavy, inert, insoluble liquids of high boiling-point; they have pleasant odours, and are

volatile with steam, and like the isomeric nitrites, are somewhat explosive. *Nitromethane*,  $\text{CH}_3\cdot\text{NO}_2$  (Victor Meyer, 1872), boils at  $101^\circ$ , and *nitroethane*,  $\text{C}_2\text{H}_5\cdot\text{NO}_2$ , at  $114^\circ$ .  *$\alpha$ -Nitrohexane*,  $\text{CH}_3\cdot[\text{CH}_2]_4\cdot\text{CH}_2\text{NO}_2$ , boils at  $181^\circ$ ;  *$\beta$ -nitrohexane*,  $\text{CH}_3\cdot[\text{CH}_2]_3\cdot\text{CH}(\text{NO}_2)\cdot\text{CH}_3$ , which resembles aniseed in odour, boils at  $176^\circ$ . When pure, the nitro-paraffins are neutral, non-conducting liquids, having little chemical activity.

In particular they are not affected by bromine water or nitrous acid, nor coloured by ferric chloride, and they do not form diazonium compounds (see § 232). They are converted into the corresponding primary amines by reducing agents, and the primary nitro-compounds, derived from the primary alcohols, are hydrolysed to the corresponding fatty acids by concentrated hydrochloric acid, the nitrogen being eliminated as hydroxylamine; nitromethane thus yields methylamine and formic acid, and  *$\alpha$ -nitrohexane* gives  *$\alpha$ -hexylamine* and *n-caproic acid*.



The reduction to amines shows that the nitrogen atoms are linked to the alkyl groups, and the general inertness of the nitro-compounds shows that they are essentially saturated compounds, and contain the saturated nitro-group,



**232. The Isonitro-Paraffins.**—Although nitromethane is quite neutral, it is at once converted by alcoholic sodium ethoxide into a crystalline metallic derivative, the molecular formula of which is that of nitromethane in which one of the hydrogen atoms is replaced by sodium; on carefully decomposing this sodium compound with dilute sulphuric acid the nitro-compound is to a certain extent recovered unchanged, although much is lost by hydrolysis. But if this decomposition be effected at a low temperature, the liberated nitro-compound has temporarily quite different properties.

It is now acid in character, and an electrolyte, it is coloured red by ferric chloride, it enters into combination with nitrous acid, forming a nitrolic acid (§ 234), and it at once combines with diazonium compounds (§ 258) at  $0^\circ$ . These properties, however, are quite transient, and the nitro-compound soon relapses into its normal inactivity.

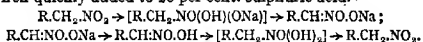
This remarkable change in properties is intelligible if a labile acid isomeride is temporarily formed, of which the sodium compound is the salt (Nef, 1894; compare Potassium Cyanide and Formonitrile, § 205).

*Sodium isonitromethane*,  $\text{CH}_2\cdot\text{NO}\cdot\text{ONa}$ , is a white crystalline substance, which is converted by dilute acids at a low tempera-

ture into *iso-nitromethane*,  $\text{CH}_3\text{NO.OH}$ , an unstable liquid which is rapidly isomerised to the stable or normal nitromethane.

The presence of a hydroxyl group attached to one of a doubly-linked pair of atoms accounts both for the acidity and the unsaturated character of the compound (compare Acrylic Acid, § 132). Both nitromethane and isonitromethane are dehydration products of *methyl-nitroic acid*,  $\text{CH}_3\text{NO(OH)}_2$  (Hantzsch, 1899); the iso-nitroparaffins and nitroic acids are too unstable to be definitely isolated, but analogous aromatic compounds have been prepared in the crystalline state (see Phenyl-nitromethane, § 281).

The conversion of nitromethane into sodium iso-nitromethane, in spite of its neutral character, is thus due to the transient formation of an additive compound or *nitroate* which is at once dehydrated to the sodium salt of the iso-compound. The hydrolysis of the nitro-paraffins to fatty acid and hydroxylamine is explained by the formation and dehydration of analogous additive products; the iso-nitroparaffins are not hydrolysed in this manner, for sodium iso-nitroethane yields aldehyde and nitrous oxide when quickly added to 20 per cent. sulphuric acid.

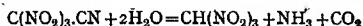


All the primary and secondary nitro-paraffins (namely, those derived from the primary and secondary alcohols) form sodium derivatives, and labile iso-nitro-compounds, but the tertiary nitro-compounds, such as *tertiary nitrobutane*,  $\text{CMe}_3\text{NO}_2$ , do not do so, as there is no alkyl hydrogen which can be eliminated as water (compare Ethyl methyl-ethyl-acetoacetate, § 145).

**233. Complex Nitro-Compounds.**—Dinitromethane, trinitromethane and tetranitromethane bear the same relation to nitromethane as methylene chloride, chloroform and carbon tetrachloride to methyl chloride, but unlike the halogen compounds, they cannot be prepared directly.

*Dinitromethane*,  $\text{CH}_2(\text{NO}_2)_2$ , is a very unstable oil; its potassium derivative is formed by reducing *di-bromonitromethane*,  $\text{CBr}_2(\text{NO}_2)_2$ , with potassium arsenite. The dibromo-compound is obtained by destructively nitrating such brominated compounds as dibromolevulinic acid (§ 151). The metallic derivatives of dinitromethane are explosive; they are salts of the acid *isodinitromethane*,  $\text{CH}(\text{NO}_2)_2\text{NO.OH}$ .

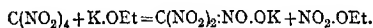
*Trinitromethane* or *nitroform*,  $\text{CH}(\text{NO}_2)_3$ , is a crystallisable, explosive oil; its ammonium derivative is formed by simple hydrolysis of *trinitroacetoneitrile*,  $\text{C}(\text{NO}_2)_3\text{CN}$ , the resolution being analogous to that of trichloroacetic acid into chloroform and carbon dioxide.



Nitroform is immediately converted by alkalis into salts of *isonitroform*,  $\text{C}(\text{NO}_2)_2\text{NO.OH}$ , or its hydrate, *dinitromethyl-nitroic acid*,  $\text{CH}(\text{NO}_2)_2\text{NO(OH)}_2$ ; this is a very strong acid

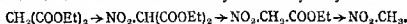
comparable with the mineral acids, as it is not entirely reconvertible into the stable, neutral nitroform, even by concentrated hydrochloric acid. Nitroform, like chloroform, is neutral substance, so that nitro-groups, like chlorine atoms, exert their powerful acidifying influence only on hydroxylic hydrogen, and have no influence on hydrogen atoms which are directly connected with carbon.

*Tetranitromethane*,  $C(NO_2)_4$ , obtained by further nitrating nitroform with fuming nitric and sulphuric acids, is a stable crystallisable liquid which can be distilled unchanged; it is quite neutral, and does not form salts, as it contains no hydrogen (compare Tertiary Nitrobutane, § 232). It is hydrolysed by alcoholic potash to potassium isonitroform and ethyl nitrate.

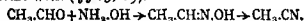


The corresponding *nitrochloroform* or *chlorpicricum*,  $CCl_3.NO_2$  (Stenhouse, 1848), a pungent heavy liquid boiling at  $113^\circ$ , is formed either by nitrating chloroform or chlorinating nitromethane, but is most readily prepared by distilling a cream of picric acid (§ 295) and bleaching powder with steam; it is converted into guanidine by ammonia.

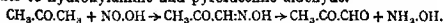
Various other types of aliphatic nitro-compounds have been prepared. The nitro-aliphatic acids are too unstable to be isolated, but their esters are known. *Ethyl nitrate*,  $CH_3(NO_2).COOEt$  (Lewkowitsch, 1880), a colourless liquid boiling at  $152^\circ$  or at  $95^\circ/10\text{ mm.}$ , is prepared either from ethyl iodacetate and silver nitrite, or by nitrating ethyl malonate; in the latter case, *ethyl nitromalonate* is an intermediate product. Ethyl nitrate is converted into nitromethane by further hydrolysis.



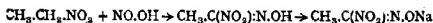
**234. Oximes and Allied Compounds.**—The formation of acetaldoxime and acetoxime by condensation of aldehyde and acetone with hydroxylamine, and the conversion of the aldoxime into the corresponding nitrile have been already dealt with (§§ 85, 89).



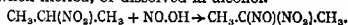
Aldoximes are also formed by the action of nitrous acid on the methy ketones; acetone thus yields isonitrosoacetone. *Isonitroso-acetone* or *pyroracemic aldoxime*,  $CH_3.CO.CH.N.OH$ , is a crystalline substance, melting at  $65^\circ$ , which is hydrolysed by hydrochloric acid in the normal manner to hydroxylamine and pyroracemic aldehyde.



Substances which are both oximes and nitro-compounds are similarly formed by the action of nitrous acid on the alkali isonitro-paraffins; nitrous acid has no action on the primary nitro-paraffins. *Isonitroso-nitro-ethane* or *ethyl-nitrolic acid*,  $CH_3.C(NO_2).N.OH$  (V. Meyer, 1875), is a colourless crystalline substance, which from the influence of the nitro-group on the hydroxyl is distinctly acid in reaction; in common with many nitro-compounds it is sweet (compare Nitrobenzene, § 246). Although the acid itself is colourless, its alkali salts are deep crimson in colour (compare Nitrophenols, § 294).

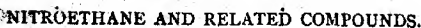


By the action of nitrous acid on the secondary-alkyl nitro-compounds, however, isomeric nitroso-nitro-compounds are formed; secondary propyl alcohol thus yields nitroso-nitro-propane. *Propyl pseudo-nitrole* or *nitroso-nitro-propane*,  $\text{NO.CMe}_2\text{NO}_2$  (V. Meyer, 1875), is a neutral crystalline substance; the acidifying influence of the nitro-group does not extend to the methyl hydrogen. It is colourless when solid, but assumes a deep blue colour when melted, or dissolved in alcohol.



The nitro-compounds of tertiary alkyl radicals are not affected by nitrous acid, so that the class of an alcohol is readily determined by means of these reactions. The alcohol is converted into the iodide, the latter into the nitro-compound by boiling with silver nitrite; and the nitro-compound is mixed, first with potash solution and potassium nitrite, and then with a little dilute sulphuric acid. If the alcohol is primary, a red colour is developed; if it is secondary, a blue colour appears; whilst if it is tertiary, the product remains colourless (V. Meyer).

**235. Synopsis.**—In addition to the alkyl nitrates and nitrites, in which the alkyl is linked to oxygen, there are various oxygen-nitrogen compounds, such as the nitro- and nitroso-compounds, and the oximes, in which the alkyl is directly linked to nitrogen.

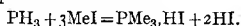




## CHAPTER XLII

### COMPOUNDS OF PHOSPHORUS, SULPHUR, METALS, ETC.

**236. The Phosphines.**—The remaining elements of the nitrogen group form alkyl compounds, which are analogous to the amines, and bear much the same relation to them as the elements themselves to nitrogen. The tertiary phosphines, for example, are made by the interaction of the alkyl iodides with hydrogen phosphide or phosphonium iodide, in the same way as the amines; and by the interaction of the zinc alkyls and phosphorus trichloride.



*Trimethylphosphine*,  $\text{PMe}_3$  (Hofmann, 1857), is an insoluble and highly refractive liquid, which boils at  $42^\circ$ , and has an extremely repulsive odour, except when very dilute. Like trimethylamine, it readily combines with methyl iodide, forming an "ammonium" iodide.

*Tetramethylphosphonium iodide*,  $\text{PMe}_4\text{I}$ , is a crystalline substance which resembles the corresponding nitrogen compound, and is similarly converted into a caustic hydroxide by moist silver oxide.

*Tetramethylphosphonium hydroxide*,  $\text{PMe}_4\text{OH}$ , is a deliquescent, crystalline, and highly alkaline solid, which, like the ammonium compound, forms well defined salts with acids, precipitates metallic hydroxides, and expels ammonia from its salts. The tetramethylphosphonium radical, like the corresponding nitrogen derivative, thus simulates the alkali metals.

The primary and secondary phosphines are formed by a special method, by the action of the alkyl iodides on phosphonium iodide in presence of zinc oxide, but resemble the tertiary compounds in character.

*Methyl phosphine*,  $\text{Me.PH}_2$  (Hofmann, 1871), is a spontaneously inflammable gas, condensing at  $-14^\circ$ , and *dimethyl phosphine*,  $\text{PHMe}_2$ , is a similar liquid, boiling at  $25^\circ$ . Both, like the tertiary base, form phosphonium salts with acids, but their basicity is not so pronounced as that

## 237] *Compounds of Phosphorus, Sulphur, Metals* 307

of the amines; they are insoluble in water also, and on account of the greater readiness of phosphorus to assume the pentavalent condition are easily oxidised. The tertiary compounds behave in fact like divalent metals, forming additive oxides, chlorides, sulphides, etc.

**237. The Arsines, Stibines, and Bismuthines.**—The primary and secondary alkyl derivatives of the higher members of the nitrogen group are scarcely known, but the tertiary and quaternary compounds resemble those of nitrogen and phosphorus; the tertiary arsenic compound is formed by the interaction of zinc methyl and arsenious chloride, or of sodium arsenide and methyl iodide.

*Trimethylarsine*,  $\text{AsMe}_3$  (Hofmann, 1855), is a colourless insoluble liquid, which boils at  $200^\circ$ , and is very repulsive in odour. It combines with methyl iodide in the same way as the amine and phosphine, forming a crystalline *tetramethylarsonium iodide*,  $\text{AsMe}_4\text{I}$ , which is similarly convertible into a caustic *tetramethylarsonium hydroxide*,  $\text{AsMe}_4\text{OH}$ . On the other hand, it does not form salts with acids, and its tendency to behave as a divalent metallic radical, and form additive compounds with chlorine, etc., is much more marked than with the phosphine.

The dimethyl-arsine radical, *cacodyl*, plays the part of an alkali metal, and may be considered as an Organic analogue of the electro-positive elements (Bunsen, 1843). Its oxide is formed by dry-distilling white arsenic with sodium acetate.



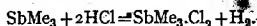
*Cacodyl oxide*,  $(\text{AsMe}_2)_2\text{O}$  (Cadet, 1760), is a colourless liquid, boiling at  $160^\circ$ , and having a most objectionable odour (*κακοδῆς*). In its chemical actions it is intermediate to the alkali and alkyl oxides. On the one hand it is converted by hydrochloric acid into *cacodyl chloride*,  $\text{AsMe}_2\text{Cl}$ , a liquid which boils at  $100^\circ$ , but resembles the alkylchlorides in forming a sparingly soluble platinichloride; on the other hand by heating with zinc dust it is converted into (di)cacodyl, in the same way as methyl iodide into dimethyl.

*Cacodyl*,  $\text{As}_2(\text{CH}_3)_4$  (Bunsen, 1842), is a colourless, insoluble and spontaneously inflammable liquid, which boils at  $170^\circ$ , and freezes at  $-6^\circ$ . Like the oxide and other compounds its odour is very repulsive.

In the antimony and bismuth compounds, which are formed in the same way as those of arsenic, the pseudo-bivalent character of the radicals is more pronounced, and there is a still greater tendency to form additive compounds with the negative elements rather than with acids.

*Trimethylstibine*,  $\text{SbMe}_3$ , is a liquid, which on the one hand is convertible into *tetramethylstibonium iodide*,  $\text{SbMe}_4\text{I}$ , and a caustic *tetramethylstibonium hydroxide*,  $\text{SbMe}_4\text{OH}$ , whilst

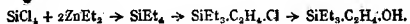
on the other hand, its metallic character is so marked, that it expels hydrogen from hydrochloric acid, in the same way as a bivalent metal, such as zinc.



*Trimethylbismuthine*,  $\text{BiMe}_3$ , the highest member of the nitrogen-alkyl series, corresponding with the unknown bismuth trihydride, is a very unstable liquid, which explodes when heated. It does not appear to combine directly with oxygen or chlorine, nor does it form quaternary compounds with alkyl iodides; in its behaviour with acids, it resembles the metallic alkyl compounds, being resolved into a bismuth salt and methane.

**238. The Metallic and other Alkyl Compounds.**—Most of the elements form alkyl compounds.\* The silicon derivatives are of especial interest, as they closely resemble the paraffins, silicon being the element most closely allied to carbon. Silicon tetrethyl is made by heating silicon chloride with zinc ethyl in an inert atmosphere, and fractionating the product.

*Silicon tetrethyl* or *silicononane*,  $\text{Si}(\text{C}_2\text{H}_5)_4$  (Friedel, 1865), is a light, spontaneously inflammable liquid, which boils at  $160^\circ$ , and resembles light petroleum in odour. Apart from its ready oxidability it closely resembles nonane in its chemical actions; it is stable towards nitric acid, however, and is converted by chlorine into a substitution product, *silicononyl chloride*,  $\text{SiEt}_3\text{C}_2\text{H}_4\text{Cl}$ , a liquid which boils at  $185^\circ$ , and resembles the alkyl chlorides. This, when boiled with potassium acetate solution, is converted into the corresponding *acetate*,  $\text{SiEt}_3\text{C}_2\text{H}_4\text{OAc}$ , a liquid boiling at  $214^\circ$ , which is resolved by alkalies in the normal manner, into acetic acid and the corresponding alcohol. *Silicononyl alcohol*,  $\text{SiEt}_3\text{C}_2\text{H}_4\text{OH}$ , is a liquid of camphor odour, which boils at  $190^\circ$ , and like the purely carbon alcohols is converted by sodium into a solid sodium alkyl-oxide.



Silicon thus resembles carbon in its power of binding carbon atoms to stable aggregates, but its power of combining with itself is very limited; the longest silicon "chain" at present known contains but three silicon atoms.

The less basic metals, such as tin and lead, share this power to a certain extent, and thus distantly resemble the nitrogen elements in their combinations, but as the more positive metals are approached, and the oxidability of the alkyl compounds becomes more marked, their power of forming "ammonium" hydroxides decreases.

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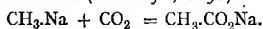
\* For Iodonium and Oxonium compounds, see §§ 264, 409.

The asymmetrical quaternary iodides of silicon, tin and lead, namely those in which the nucleal atom is united to four different groups, are resolvable into optically active isomerides by the camphorsulphonic method (Pope, 1900).

*Tin tetrethyl*,  $\text{SnEt}_4$  (Ladenburg, 1872), is a liquid of pleasant odour, which boils at  $181^\circ$ , and is not spontaneously inflammable. It is converted by hydrochloric acid into ethane and *triethylstannic chloride*,  $\text{SnEt}_3\text{Cl}$ , and this by caustic alkalis into the corresponding hydroxide; *triethylstannic hydroxide*,  $\text{SnEt}_3\text{OH}$ , is an alkali resembling the ammonium hydroxides, but is less soluble and energetic. Lead and mercury form similar derivatives; *ethylmercuric hydroxide*,  $\text{HgEt.OH}$ , is a viscid, alkaline, and exceedingly poisonous liquid, which forms stable salts with acids.

The alkyl compounds of the highly positive metals do not form such hydroxides. *Zinc methyl*,  $\text{ZnMe}_2$  (§ 91) is hydrolysed to methane and zinc oxide even by water, and the analogous *aluminium trimethyl*,  $\text{AlMe}_3$ , and *magnesium diethyl*,  $\text{MgEt}_2$ , behave in a similar manner.

The alkyl compounds of the alkali metals are not known in a pure state. *Sodium methyl*,  $\text{NaMe}$ , appears to be formed when sodium is digested with zinc methyl, for metallic zinc is precipitated, and the resulting liquid absorbs carbon dioxide, forming sodium acetate (Wanklyn, 1858).



The valency of the various metals follows from the vapour density of these volatile alkyl derivatives; it was their discovery which gave rise to this idea (E. Frankland).

**239. The Sulphides and Sulphonium Compounds.**—When ethyl bromide is boiled with potassium hydrosulphide solution, it is converted into ethyl hydrosulphide, the action being precisely parallel to the hydrolysis of the bromide by caustic soda.



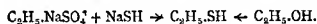
The sulphide is best prepared by distilling ethyl sodium sulphate with a solution of caustic soda which has been saturated with sulphuretted hydrogen. The product passes over with the steam and forms an oily layer on the water. It is purified by shaking with mercury, with which it forms a crystalline compound, and decomposing the washed and dried crystals with hydrogen sulphide.

*Ethyl hydrosulphide* or *mercaptan*,\*  $\text{C}_2\text{H}_5\text{SH}$  (Zeise, 1834), is a light, insoluble liquid, boiling at  $36^\circ$ . Its odour resembles

\* Mercurium captans.

that of garlic, but is more offensive. The hydrogen of the hydrosulphyl group is replaceable by metals, like that of hydroxyl, but the compounds thus formed, such as *mercury mercaptide*,  $\text{Hg}(\text{SEt})_2$ , are much more stable than the metallic alkyl oxides.

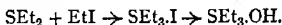
The constitution of mercaptan follows from the mode of its preparation, and is confirmed by its formation from alcohol by the action of phosphorus pentasulphide. The homologous alkyl compounds are similar liquids.



The sulphide corresponding with mercaptan is formed by heating ether with phosphorus pentasulphide, or ethyl bromide with alcoholic potassium sulphide. *Ethyl sulphide*,  $\text{Et}_2\text{S}$ , is a liquid which resembles mercaptan physically, but boils at  $91^\circ$ .

The corresponding *allyl sulphide*,  $(\text{C}_3\text{H}_5)_2\text{S}$ , made in a similar manner from allyl iodide, is, as already mentioned, identical with oil of garlic. *Methyl ethyl sulphide*,  $\text{MeEtS}$ , from sodium mercaptide and methyl iodide, boils at  $77^\circ$ . More complex sulphides are also known. Thus by the oxidation of mercaptan with iodine, *ethyl disulphide*,  $\text{Et}_2\text{S}_2$ , is formed, and by the interaction of mercaptan with the aldehydes and ketones, compounds termed *mercaptals* and *mercaptols* are obtained, which are sulphur analogues of the acetals. *Ethylidene mercaptal*,  $\text{CH}_3\cdot\text{CH}(\text{SEt})_2$ , is an oily liquid, boiling at  $186^\circ$ .

Bivalent sulphur resembles oxygen in its combinations. Quadrivalent sulphur on the other hand behaves in the same way as the elements of the nitrogen series, and forms compounds akin to those of the phosphonium group. Ethyl sulphide combines with ethyl iodide, forming an "ammonium" iodide, which is converted by caustic alkalies into an alkaline hydroxide.



*Triethylsulphonium iodide*,  $\text{SEt}_3\text{I}$ , is a crystalline substance, which resembles the corresponding compounds of the phosphorus group. *Triethylsulphonium hydroxide*,  $\text{SEt}_3\text{OH}$ , is a deliquescent crystalline substance, which forms salts with acids, expels ammonia from its salts, absorbs carbon dioxide, and behaves in every respect as an alkali. Thus even sulphur is converted into a positive radical by alkyl.

The alkyl sulphides combine additively with bromoacetic acid, forming sulphonium bromides. These yield anhydrides when hydrolysed with moist silver oxide, which resemble betaine in constitution, and are hence termed *thetines*\* (Crum Brown, 1873); they are neutral crystalline substances having feeble basic properties.

\* Thiobetaines.

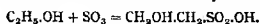


soluble crystalline substance, which melts at  $162^{\circ}$ , and is used instead of chloral as a hypnotic.

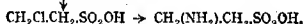
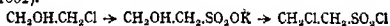
Although most of the proteins are sulphur compounds, comparatively few natural organic sulphur derivatives have been isolated. One of the chief of these is taurine, a neutral aminoid substance, which is obtained by hydrolysis of the *taurocholic acid* of ox-bile.

*Taurine* or *amino-isethionic acid*,  $\text{CH}_2(\text{NH}_2)\text{CH}_2\text{SO}_3\text{OH}$  (Gmelin, 1824), is a crystalline substance, melting at  $240^{\circ}$ . Like glycine, it is indifferent to alkalis and acids, and that it is a primary amine is proved by its conversion by nitrous acid into the corresponding hydroxy-compound, isethionic acid, with elimination of nitrogen.

*Isethionic acid*,  $\text{CH}_2\text{OH}\cdot\text{CH}_2\cdot\text{SO}_3\text{OH}$ , is a viscid liquid which crystallises only with difficulty: it can be made synthetically by dissolving sulphuric anhydride in well cooled alcohol, and also from synthetic taurine.



Taurine can be synthesised from ethylene. By the interaction of ethylene chlorhydrin with potassium sulphite, *potassium isethionate* is formed, and this is converted by phosphorus pentachloride into *chloroethyl-sulphonic chloride*. This substance, like chloracetyl chloride, is only partially hydrolysed by cold water, the alkyl chloride remaining untouched, and the *chloro-sulphonic acid* thus obtained is converted by ammonia into the amino-acid, taurine, the constitution of which is thus demonstrated (Kolbe, 1862).



**241. Synopsis.**—Phosphorus and the other elements of the nitrogen group form alkyl derivatives, which resemble the amines and ammonium compounds, but are progressively less stable. Most of the elements form such compounds. The sulphur alkyl derivatives are oxidisable to stable sulphones and sulphonic acids, which are derivatives of sulphurous acid in which the alkyl is linked directly to sulphur.

PART III  
**Aromatic or Ring Compounds**

SECTION XI  
**BENZENE AND THE PHENYL RADICAL**

CHAPTER XLIII

BENZENE AND ITS SUBSTITUTION PRODUCTS

**242. The Benzenoid Group of Compounds.**—Although the compounds considered in the preceding sections are derived from the paraffins and related hydrocarbons, and can in many cases be made from them, the processes are rarely economical, and, as a rule, are both wasteful and tedious.

A very large and important group has now to be dealt with, the members of which are not only derived from the corresponding hydrocarbons, but in the majority of cases are most conveniently and economically made from them; most of the organic drugs and dye-stuffs are members of this group, which, owing to its technical importance and ease of manipulation, has been more studied than any other.

The earlier known, naturally occurring members of the group were classed together as the aromatic compounds, because of their fragrant, aromatic odour, and further investigation showed that the apparently empirical classification was justifiable chemically. These compounds are more or less complex derivatives of a single hydrocarbon, benzene, and constitute the benzenoid group of compounds (Kekulé, 1865); they are made either from benzene itself, or substances closely related to it.

**243. Separation of Benzene from Coal-Tar.**—Benzene was first found, together with butylenes (§ 106), in the liquid which condenses from compressed oil-gas (Faraday, 1825); its present name being derived from that of benzoic acid (§ 267).



from which it is readily prepared (Mitscherlich, 1867). It is also made synthetically by passing acetylene through a red-hot tube (Berthelot, 1870), and is present in American petroleum.

The chief source of benzene is coal-tar, the black, viscous liquid which is obtained on distilling coal (Mansfield, 1848); coal-gas contains methane and ethylene, and it is probable that the more complex hydrocarbon is here also formed synthetically, by the action of the red-hot retort walls on these simple hydrocarbons.

Coal-tar is a complex mixture containing many valuable products—benzene and homologous hydrocarbons; phenols (§ 254) and solid hydrocarbons, such as naphthalene (§ 369) and anthracene (§ 375); these are roughly separated on a manufacturing scale by a single fractional distillation from large iron stills. The head fraction, distilling below  $150^{\circ}$ , consists principally of benzene and its near homologues; it constitutes about 14 per cent. of the tar, and is termed light oil, as it floats on water.

To isolate the benzene, the crude oil is shaken with concentrated sulphuric acid to remove olefines and thiophene (§ 406), and basic impurities such as pyridine (§ 387). Phenols are dissolved out by shaking with caustic soda and the dried liquid is fractionated in a column apparatus; the fraction  $80-110^{\circ}$  contains 65 to 75 per cent. of benzene, whilst the higher fractions consist principally of homologous hydrocarbons—toluene, the xylenes, etc. After further fractionation, and heating with alcoholic potash, or saturating with moist ammonia gas, to remove carbon disulphide, the dried, rectified benzene is purified from toluene and paraffins by freezing, as in the purification of acetic acid.

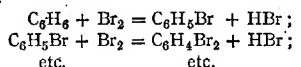
**Benzene**,  $C_6H_6$  (Faraday, 1825), is a mobile liquid, having a pleasant characteristic odour; it freezes at  $5^{\circ}$ , boils at  $80^{\circ}$ , and has a specific gravity of 0.874 at  $20^{\circ}$ . Benzene is insoluble in water, but miscible with alcohol and ether in all proportions, and like ether dissolves fats, resins, phosphorus, etc.; it is very inflammable, and burns with a luminous, smoky flame.

Pure benzene does not darken cold concentrated sulphuric acid, nor immediately decolorise a drop of bromine water, nor does it reduce cold alkaline permanganate; in these respects it differs markedly from the olefines (§ 104).

**244. The Bromobenzenes.**—Benzene is a very stable substance; it can be boiled with oxidising mixtures, such as chromic acid or acid permanganate, without being appreciably decomposed, and in this respect is practically as stable as the paraffins. On the other hand, it is much more readily chlorinated and brominated, and under certain conditions is also rapidly attacked by sulphuric and nitric acids (compare §§ 78, 231).

When it is warmed with bromine in a reflux apparatus, pre-

ferably in presence of a carrier (§ 114), hydrogen bromide is evolved in large quantities and bromo-substitution products are formed.



As in all such cases, the operation is much accelerated by the presence of the carrier—iodine, aluminium chloride, or iron filings (ferric bromide); and as in this case the action is apt to be violent, the bromine should be added gradually, preferably from a tap-funnel at the upper end of the condenser; the hydrogen bromide is collected in a water-trap (Fig. 18, § 114).

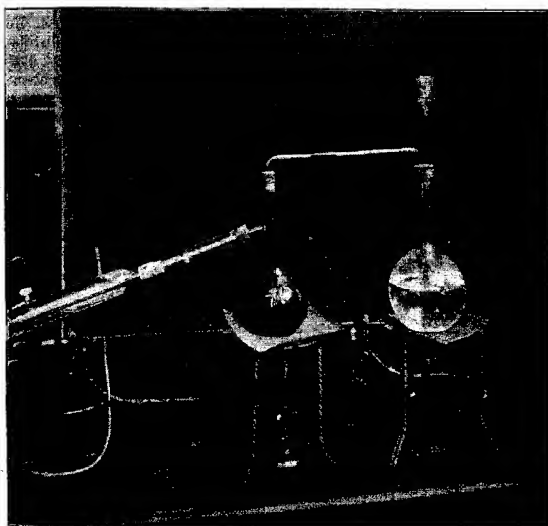


Fig. 21.—Distillation with Steam.

As soon as the bromine vapour disappears from the flask, the product is washed with water and dilute alkali and then distilled with steam (Fig. 21). Some unchanged benzene first passes over, but as soon as the oily drops sink to the bottom of the water, the distillate is collected apart; towards the end of the distillation crystals of dibromobenzene appear in the condenser. The heavy bromobenzene is then separated from the supernatant water, and fractionated; the minute quantity of dissolved water passes over with the first fraction of the distillate, rendering it turbid, whilst the last fractions contain dibromobenzenes, etc.

The solid dibromo-compound is purified by recrystallisation from alcohol. The product from the latter part of the steam distillation is dissolved in hot alcohol, and the solution cautiously diluted with hot water until it is slightly but permanently turbid. It is then filtered, either through a hot funnel, or a "pleated" filter in a neckless funnel; the dibromobenzene crystallises out quickly as the solution cools, and is dried on a porous plate.

*Bromobenzene*,  $C_6H_5Br$  (Couper, 1857), is a heavy, colourless, insoluble liquid, which boils at  $157^\circ$ , and has a specific gravity of 1.52 at  $0^\circ$ ; its odour is aromatic and pleasant (compare § 280). (*para*-)*Dibromobenzene*,  $C_6H_4Br_2$ , is a colourless, crystalline solid, which melts at  $89^\circ$  and boils at  $219^\circ$ .

*Hexabromobenzene*,  $C_6Br_6$ , a crystalline substance melting at about  $315^\circ$ , is similarly obtained when a large excess of bromine is employed; and various *tri*-, *tetra*- and *penta*bromobenzenes can also be prepared.

Although formed from benzene in the same way as ethyl chloride, etc., from ethane, the bromobenzenes differ markedly from the corresponding paraffinoid compounds in that their halogen is much less active; boiling alkalies do not affect them (§ 22), and they remain unchanged when heated with alcoholic ammonia (§ 58); potassium cyanide does not displace their halogen (§ 63), nor is this withdrawn by boiling with silver acetate (§ 45).

On the other hand, the aromatic haloids are slowly reduced to the hydrocarbon when their alcoholic solution is digested with sodium amalgam; and the halogen is removed from bromobenzene by boiling with sodium, when a complex hydrocarbon, diphenyl, is formed, as in the synthesis of butane from ethyl iodide (§ 78). Like the halogen alkyl compounds, bromobenzene also combines directly with metallic magnesium, preferably in presence of ethyl or amyl ether, forming *magnesium phenyl bromide*,  $C_6H_5.MgBr$ , a compound of considerable importance in synthesis.

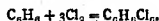
**245. Other Halogen Benzenes: Benzene Hexachloride.**—The chloro-derivatives corresponding with the bromobenzenes can be made in a similar manner. *Chlorobenzene*,  $C_6H_5Cl$ , which boils at  $132^\circ$ , is an aromatic liquid resembling bromobenzene.

Some of the iodo-compounds can also be formed by direct substitution, provided that iodic acid is present to oxidise the resulting hydrogen iodide; these compounds, however, together with fluorobenzene, are more conveniently made through aniline, by the diazonium interaction (§ 260). *Fluorobenzene*,  $C_6H_5F$ , boils at  $86^\circ$ ; *iodobenzene*,  $C_6H_5I$ , at  $188^\circ$ .

Benzene thus behaves with the halogens under ordinary conditions in the same way as the paraffins, that is to say, essentially as a saturated compound; the only difference of importance is that the various substitutions are more easily effected, and the products correspondingly more stable and

Under special conditions, however, it is capable of acting as an unsaturated hydrocarbon, forming additive compounds such as benzene hexachloride.

When chlorine saturated with benzene vapour is exposed to direct sunlight, the walls of the vessel become coated with a crystalline additive compound. The same compound is readily obtained by passing chlorine into 1 per cent. caustic soda, on which the benzene is floating; it is purified by distillation with steam. In this respect benzene resembles the unsaturated hydrocarbons.



*Benzene hexachloride*,  $\text{C}_6\text{H}_6\text{Cl}_6$  (Faraday, 1825), is a crystalline substance, melting at  $157^\circ$ ; although formed in the same way as the additive olefine and acetylene chlorides it is much less stable, and is readily resolved by heat into hydrogen chloride and trichlorobenzene.

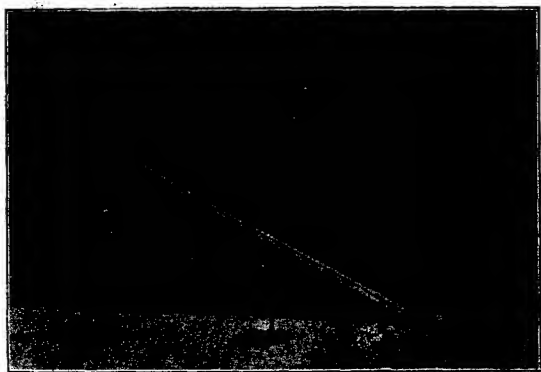
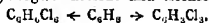
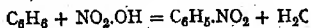


Fig. 22.—Distillation of Liquid of High Boiling Point.

**246. Nitrobenzene.**—The action of nitric acid on benzene is similar to that of the halogens, various substitution products being formed according to the experimental conditions; the mononitro-derivative is easily made by slowly pouring a cold mixture of concentrated nitric and sulphuric acids, with constant agitation, into cold benzene.



Much heat is evolved, and the temperature must not be allowed to rise above  $45^\circ$ ; on the other hand, the liquid should not be kept too cool, or the action may not take place at all. The brown, oily product is heated with the acid mixture on a water-bath for half an hour; after well

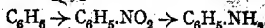
the mixture (§ 22), any unchanged benzene is evaporated off. If the temperature rises too high in the initial reaction, dinitro-

**Nitrobenzene**,  $C_6H_5NO_2$  (Mitscherlich), is an almost colourless, oily liquid, which has a rank, aromatic odour recalling that of almond essence, and when dilute, a very sweet taste; it is poisonous, and the vapour should not be inhaled. Nitrobenzene boils at  $209^\circ$ , and freezes to a crystalline solid, melting at  $5^\circ$ ; its specific gravity is 1.21 at  $20^\circ$ ; it is sparingly soluble in water, but freely in organic solvents.

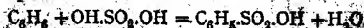
The nitro-compound is thus formed from the hydrocarbon in the same way as the halogen-compounds, namely by direct substitution of hydrogen; and benzene again behaves essentially as a saturated compound. As the hydrogen is replaced by the nitro-group,  $NO_2$ , the operation is known as nitration.

The action is not without analogy amongst the aliphatic compounds, for some of the higher paraffins are nitrated in a similar manner (§ 231). The aromatic nitro-compound to a certain extent resembles the tertiary nitroparaffins (§ 231) in its behaviour, particularly in its stability towards hydrolytic agents.

Although nitrobenzene slowly turns brown on exposure to light, it is essentially a stable substance; it is not hydrolysed by alkalis, and whilst it interacts with halogens, and under certain conditions with nitric and sulphuric acids, this is because of further substitution (§ 292). Its stability is explained by the direct linkage of the nitrogen to the benzene-carbon nucleus, which is proved by its conversion into the corresponding amino-compound, aniline (§ 249) by ordinary reducing agents.



**247. Benzene Sulphonic Acid.**—When benzene is gently heated in a reflux apparatus with concentrated sulphuric acid, or better, shaken with the fuming acid, it is gradually dissolved, forming a substitution-product of a third type, benzene sulphonic acid.



The product is separated from the excess of sulphuric acid by pouring into the soluble calcium salt, in the same way as ethyl sulphate (§ 245) from the acid, and the sodium salt formed in the reaction (§ 245) can be boiled down without risk of loss of benzene, and ordinary hydrolytic agents.

## 216. BENZENESULPHONIC ACID

Benzenesulphonic acid is prepared by the action of sulphuric acid on benzene. The cold saturated solution of benzene in sulphuric acid is mixed with an equal volume of water, and the mixture is allowed to stand for 24 hours. The mixture is then poured into water, and the acid is removed by washing with water. The acid is then dried by distilling under reduced pressure.

**Benzenesulphonic acid**,  $\text{C}_6\text{H}_5\text{SO}_3\text{H}$ , is a deliquescent, crystalline substance, which melts at  $44^\circ$ , or at  $51^\circ$  when anhydrous; it is very soluble in water and alcohol, but practically insoluble in other organic solvents. It is a strong acid, and forms stable salts and esters, the latter being prepared, however, by means of the acid chloride.

The sodium and potassium salts are soluble crystalline substances; the silver salt contains water of crystallisation (compare § 31); the methyl and ethyl esters are liquids which may be distilled unchanged under low pressure; they are quickly hydrolysed by water.

The formula of the sulphonic acid shows that it is a substitution product, and not an additive compound such as is obtained by the interaction of sulphuric acid and olefines (§§ 104, 106); so that here also benzene behaves as a saturated hydrocarbon. The operation is known as **sulphonation**.

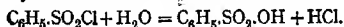
The benzenesulphonates are quite stable towards aqueous and alcoholic alkalis, a fact which again is explained, as in the case of the nitro-compound, by the assumption of a direct linkage of the sulphur atom to the benzene-carbon nucleus, which is similarly proved by reduction (see below).

The presence of acid hydroxyl is shown by the action of phosphorus haloids on benzenesulphonic acid and its salts; a vigorous action ensues when sodium benzenesulphonate is mixed with phosphorus pentachloride, resulting in the formation of benzenesulphonic chloride, an acid chloride of the same type as acetyl chloride and its analogues.



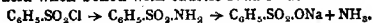
After heating on a water-bath for half an hour, the product is poured into cold water, with which it is kept in contact for a few hours, to ensure the complete decomposition of the phosphorus oxychloride. The benzenesulphonic chloride is extracted from the aqueous mixture by shaking with ether, the ethereal solution being separated by means of a funnel; the ether is removed by dropping the solution from a tap-funnel into a distilling flask, which is connected with a condenser, and heated with hot water (Fig. 24, p. 249). The residual sulphonic chloride is removed under reduced pressure, as it is decomposed to a certain extent by the action of water.

an oily liquid which boils at  $246^{\circ}$  under ordinary pressure, and freezes to a crystalline solid, melting at  $14^{\circ}$ ; its odour is pungent and unpleasant. When boiled with water, it is slowly hydrolysed to the acid.

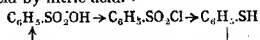


When benzenesulphonic chloride is rubbed in a mortar with excess of powdered ammonium carbonate, it is converted into the corresponding amide; after the violent action has subsided, the cooled product is washed with cold water, and recrystallised from hot alcohol (see Dibromobenzene, § 244).

*Benzenesulphonamide*,  $\text{C}_6\text{H}_5\text{SO}_2\text{NH}_2$  (Gerhardt, 1852), is a well defined, easily crystallised substance, melting at  $150^{\circ}$ . On account of the strongly acidic character of the benzenesulphonic radical, it is soluble in alkalis, but as a true amide it is hydrolysed to ammonia and the sodium salt of the acid when boiled with caustic soda solution.

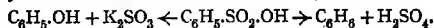


That the sulphur in these sulphonic derivatives is directly linked to carbon, is confirmed by the reduction of the chloride by sodium amalgam to phenyl mercaptan (§ 256), and by the re-oxidation of this substance to the sulphonic acid by nitric acid.



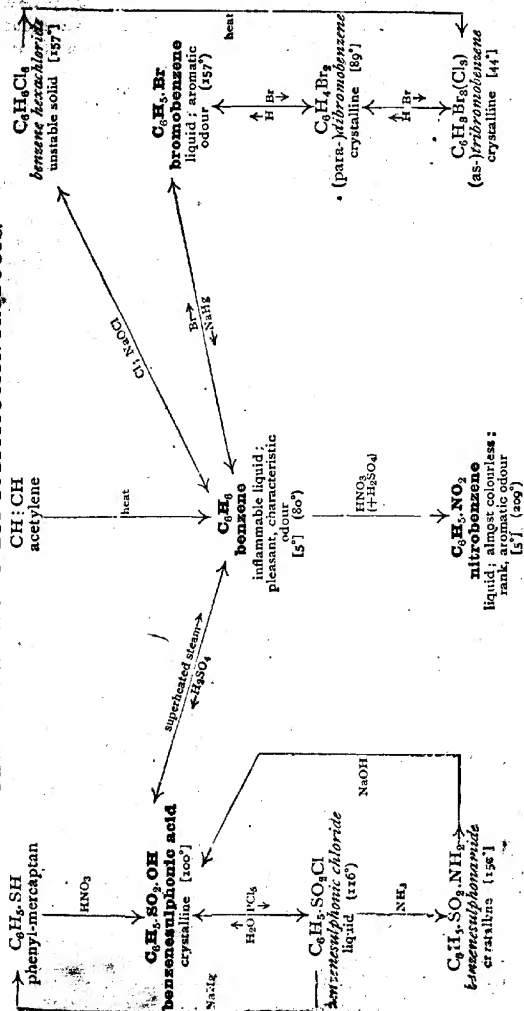
Although benzenesulphonic acid is stable towards aqueous alkalis, it is readily hydrolysed to the hydrocarbon in acid solution; the sulphonic acid or salt is dissolved in a considerable excess of concentrated sulphuric acid, and on leading steam into the heated solution, benzene distils over (Armstrong, 1884). By taking advantage of this decomposition, benzene and its homologues may be separated from olefines and paraffins.

When potassium or sodium benzenesulphonate is fused with caustic potash, it is hydrolysed to phenol (§ 255), a hydroxy-derivative of benzene.



**248. Synopsis.**—The hydrocarbon benzene is formed by the action of heat on gaseous hydrocarbons, and thus in the distillation of coal. It resembles the paraffins in stability, and in its action with halogens, but differs from them in readily forming substitution products with nitric and sulphuric acid at ordinary temperatures. It also resembles the olefines in forming additive products with halogens, but these, unlike the olefine additive compounds, are unstable.

## BENZENE AND ITS DIRECT SUBSTITUTION-PRODUCTS.



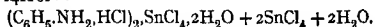
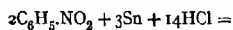


## CHAPTER XLIV

### ANILINE

**249. Aniline.**—When indigo is distilled alone, or with caustic potash, an oily basic liquid passes over, which is termed aniline, from the Portuguese name of the dye—anil (Unverdorben, 1826). The same base occurs in coal-tar, from which it may be extracted by shaking with dilute acids, with which it forms well defined, crystalline salts (Runge, 1834).

Aniline is best prepared by reducing nitrobenzene; the reduction was first effected by means of ammonium sulphide (Zinin, 1842, § 293), but is more conveniently brought about with tin and hydrochloric acid (Beilstein, 1864), or commercially, with hydrochloric acid and scrap iron. The products from the three sources are identical (Hofmann, 1844).



In the laboratory method, concentrated hydrochloric acid is cautiously poured down the condenser of a reflux apparatus containing the nitrobenzene and granulated tin, and after the brisk action has subsided, the liquid is boiled until the odour of the nitro-compound has disappeared. The base may be crystallised from the product at this stage in combination with hydrochloric acid and stannic chloride, but is best set free by excess of concentrated caustic soda, of which a large quantity is required.

The oily aniline in part rises to the surface, but much remains emulsified in the alkaline liquid; the product is therefore distilled with steam, the base being extracted with ether from the turbid distillate. The ethereal solution, dried with solid caustic soda, is then fractionated, first from a water-bath (Fig. 23) and finally over a flame. On a manufacturing scale, the aniline, which is used in large quantities in the preparation of dyes, drugs, etc., is liberated by addition of milk of lime.

Nitrobenzene may also be reduced by electrolysis its solution in alcoholic sulphuric acid; aniline is formed at the kathode, together with other products (§§ 263, 380).

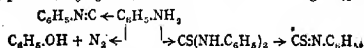
**Aniline or aminobenzene**,  $\text{C}_6\text{H}_5\text{NH}_2$  (Unverdorben, 1826), is a colourless, highly refractive liquid, which soon darkens in air, from oxidation; it boils at  $184^\circ$ , freezes to a crystalline

solid, melting at  $-8^{\circ}$ , and has a specific gravity of 1.026 at  $16^{\circ}$ ; it is sparingly soluble in water, but freely in organic solvents and in acids, and its odour is faint, but characteristic, resembling that of gas lime. Aniline is somewhat poisonous.

In its chemical actions, aniline behaves as a feeble base; it precipitates ferric hydroxide, but does not blue reddened litmus, and although it expels ammonia from ammonium salts, this is because of its inferior volatility, the action being parallel to that of silica on fused carbonates. Being a monamine, it forms additive salts with a single equivalent of acid.

The salts with mineral acids are well defined, although owing to hydrolytic dissociation, they are acid in solution. *Aniline hydrochloride*,  $C_6H_5.NH_2.HCl$ , is precipitated by hydrochloric acid in crystalline flocks, and the *nitrate*,  $C_6H_5.NH_2.HNO_3$ , is formed in a similar manner with dilute nitric acid; both can be crystallised from water.

The aminoid character of aniline is confirmed by the ready formation of crystalline double salts, such as the yellow *platinichloride* ( $C_6H_5.NH_2.HCl$ ) $_2.PtCl_4$ , and the colourless *stannichloride* ( $C_6H_5.NH_2.HCl$ ) $_2.SnCl_4$ . That it is a primary amine is shown by the usual interactions (§ 212); it is condensed to phenyl isocyanide,  $C_6H_5.N:C$  (§ 256), when heated with chloroform and alcoholic potash; with carbon disulphide and mercuric chloride it yields a pungent mustard oil,  $C_6H_5.N:CS$  (§ 256); and it is converted by nitrous acid into the corresponding hydroxy-compound, phenol,  $C_6H_5.OH$ , with liberation of nitrogen (§ 255).



Aniline is much less stable than benzene and nitrobenzene, and is slowly oxidised even by air. It is reconverted into the nitro-compound by persulphuric acid, and ultimately by alkali-

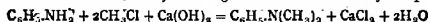


Fig 23.—Distillation of Solvent after Extraction with Ether.

line permanganate, but several intermediate products are also formed (§§ 263, 380). With bleaching solution a trace of aniline forms a characteristic violet coloration, and with sodium hypobromite a red precipitate; it is also distinguished qualitatively by the intense greenish-blue colour which is formed by adding a drop of dichromate solution to its solution in concentrated sulphuric acid, and by the bright yellow colour its salts impart to pine-wood.

**260. The Methyl-Anilines and Phenylamines.**—Aniline being a primary amine takes up three methyl groups when heated with methyl iodide, forming a quaternary ammonium compound. *Phenyl-trimethylammonium iodide*  $C_6H_5.NMe_3I$ , is a crystalline substance, which resembles the alkyl-ammonium salts (§ 214), and is similarly convertible into a crystalline, caustic ammonium hydroxide,  $C_6H_5.NMe_3.OH$ .

Intermediate compounds are also formed in this operation, but as with the aliphatic compounds, these derived amines are best made by special methods. The secondary compound, methyl-aniline, is usually prepared from methyl-acetanilide (§ 251); and the tertiary compound, dimethyl-aniline, which is used in large quantities in the dye industry, is manufactured by forcing methyl chloride at  $100^\circ$  into an agitated mixture of aniline and milk of lime, or by heating aniline with dimethyl sulphate.



*Methylaniline*,  $C_6H_5.NH.CH_3$  (Hofmann, 1850), is an oily liquid, which resembles aniline, and boils at  $193^\circ$ ; as an amine, it forms the usual additive salts, and as a secondary amine it yields with nitrous acid an oily nitroso-compound,  $C_6H_5.N(NO).CH_3$ , having a characteristic odour. When *methylaniline hydrochloride* is heated, it is transformed into the isomeric *paratoluidine hydrochloride* (§ 317).

*Dimethylaniline*,  $C_6H_5.N(CH_3)_2$  (Hofmann), is a similar liquid, which boils at  $192^\circ$ ; it is distinguished from the aliphatic tertiary amines by forming with nitrous acid a crystalline nitroso-compound (§ 296), in which the nitroso-group is linked to the hydrocarbon nucleus.

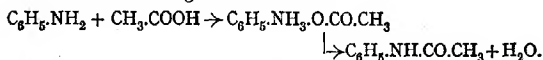
Sodium dissolves in aniline, forming *disodium-aniline*,  $C_6H_5.NNa_2$ , an amorphous and easily soluble powder; and this interacts with bromobenzene, forming *diphenylaniline* or *triphenylamine*,  $N(C_6H_5)_3$ , a neutral crystalline substance, which does not form salts with acids.

The intermediate phenylaniline, an important substance in the dye industry, is made by heating aniline hydrochloride with aniline, at  $240^\circ$ . *Diphenylamine*,  $NH(C_6H_5)_2$  (Hofmann, 1864), is a crystalline substance, which melts at  $54^\circ$ , and boils at  $302^\circ$ ; its properties are intermediate to those of the primary and tertiary amine, and it is a feeble base, its salts being decomposed by water; its solution in concentrated sulphuric acid gives an intense blue colour with nitrites. Diphenylamine forms a sodium derivative, which is converted into triphenylamine when heated with bromobenzene.

**261. Acetanilide: Anilides.**—All primary and secondary amines readily interact with acetyl chloride, and as the aromatic products of this class are well defined, stable, crystalline

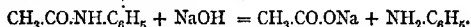
substances, they are useful in isolating the respective bases, as well as in other respects.

The aniline compound, acetanilide, is formed when aniline is mixed with acetyl chloride or acetic anhydride; a violent action occurs, and the product becomes solid. Acetanilide is more economically made by boiling aniline in a reflux apparatus with excess of glacial acetic acid.



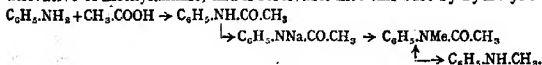
The aniline acetate at first formed is gradually dehydrated, and on fractionating the product after some hours boiling, the new product passes over, preceded by water and unchanged acid and aniline; it is collected in the same way as acetamide, and recrystallised from boiling water.

*Acetanilide* or *phenyl-acetamide*,  $\text{C}_6\text{H}_5\text{NHAc} = \text{CH}_3\text{CO.NH.C}_6\text{H}_5$  (Gerhardt, 1853), is a white crystalline substance, which melts at  $112^\circ$ , and boils at  $304^\circ$ , but unlike acetamide is only sparingly soluble in cold water; it is used as an antipyretic, under the name of *antifebrin*. As an amide, it is hydrolysed by caustic alkalies to acetic acid and the substituted ammonia, aniline.



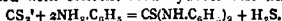
Many other anilides or aniline-amides are known; they are similar to acetanilide, and are prepared in a similar manner.

The imido-hydrogen of acetanilide is readily replaced by sodium, and when the crystalline sodium derivative is boiled with methyl iodide in toluene solution, *methyl-acetanilide*,  $\text{C}_6\text{H}_5\text{NMe.CO.CH}_3$ , is formed, a crystalline substance, which melts at  $101^\circ$ ; it is identical with the acetyl derivative of methylaniline, and is resolvable into this base by hydrolysis.



*Thiocarbanilide*, the anilide of thiocarbonic acid, is made by heating aniline and carbon disulphide with alcoholic potash; the crude anilide is precipitated by pouring the liquid into water, and is purified by washing with dilute hydrochloric acid and recrystallising from alcohol.

*Thiocarbanilide*,  $\text{CS(NH.C}_6\text{H}_5)_2$  (Hofmann, 1849), is a crystalline substance, melting at  $154^\circ$ , which is converted into phenyl mustard-oil (§ 256), when boiled with concentrated hydrochloric acid.

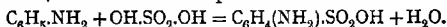


**252. Substitution Products of Aniline.**—Aniline is very readily affected by substituting-agents, and on merely adding bromine water to the solution of an aniline salt, tribromaniline is precipitated. *Tribromaniline*,  $\text{C}_6\text{H}_2\text{Br}_3\text{NH}_2$  (Fritzsche, 1842), is a crystalline solid melting at  $119^\circ$ ; it is a neutral substance,

which forms an unstable *hydrochloride*, the bromine almost neutralising the basic amino-group.

The mono- and di-bromo-compounds, which are obtained by distilling mono- and dibrom-indigo with potash (Hofmann, 1845), and in other ways (compare § 293), are intermediate in properties, the basicity of the molecule diminishing as the number of bromine atoms increases (compare Chloracetic Acids, § 116).

With sulphuric acid, aniline not only forms a sulphate, but an amino-acid akin to the aliphatic amino-acids.

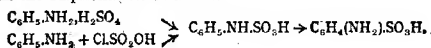


The aniline is dissolved in the concentrated acid, and the solution heated in an oil bath at 200° until the base is no longer liberated by the addition of caustic soda to a sample of the product; the mass is then poured into cold water, and recrystallised, with the addition of animal charcoal to remove colouring matter.

*Sulphanilic* or *p-aminobenzene sulphonic* acid,  $\text{C}_6\text{H}_4(\text{NH}_2)\cdot\text{SO}_3\text{H}$  (Gerhardt, 1846) is a crystalline, efflorescent substance, which chars when heated; it is used in the dye industry. The acid and basic properties of sulphanilic acid, like those of the aliphatic amino-acids, are feeble, but the acid properties are the more prominent, as the substance is soluble in alkalis and insoluble in acids.

In forming these substitution-products it is probable that in every case the amino-group is first attacked, as in the isomerisation of methyl-aniline (§ 250), the amino-hydrogen being replaced by the radical which eventually enters the benzene nucleus (Armstrong, 1887). Such unstable intermediate products have been isolated.

*Phenyl-sulphonamic acid*,  $\text{C}_6\text{H}_5\cdot\text{NH}\cdot\text{SO}_3\text{H}$  (Traube, 1890), an unstable substance which is formed by slowly adding chlorosulphonic acid to a solution of aniline in chloroform, is converted into sulphanilic acid by simply heating with sulphuric acid. As it may be formed from aniline sulphate by simple dehydration, it is evidently the precursor of sulphanilic acid in the sulphonation of aniline.



Similarly when acetanilide is treated with bleaching-powder solution it is converted into *N-chloroacetanilide* or *phenyl acetyl nitrogen chloride*,  $\text{C}_6\text{H}_5\cdot\text{NCl}\cdot\text{CO}\cdot\text{CH}_3$ , a crystalline substance melting at 91°; if this chloro-derivative is heated, or covered with cold concentrated hydrochloric acid, it is transformed into *p-chloroacetanilide*,  $\text{C}_6\text{H}_4\text{Cl}\cdot\text{NH}\cdot\text{CO}\cdot\text{CH}_3$ , a crystalline substance melting at 172°, in which the chlorine is in the benzene nucleus. Many such nitrogen chlorides, bromides and similar derivatives have been prepared (Chattaway, 1899), and all undergo similar transformations (compare also Nitranilines, § 293).

**258. Synopsis.**—Aniline is the amino-compound corresponding with nitrobenzene. In many respects it resembles the aliphatic primary amines, but it is much less basic; and as a benzene derivative readily forms substitution products.



## CHAPTER XLV

### PHENOL: THE PHENYL RADICAL

**254. Phenol.**—The second fraction obtained in the distillation of coal tar, which passes over below  $210^{\circ}$ , and is termed the middle oil, consists chiefly of a semi-acid substance, phenol, and a solid hydrocarbon, naphthalene (§ 369); it constitutes about 10 per cent. of the tar, and is approximately equal in specific gravity to water.

After the oil has been cooled, and separated from the naphthalene which crystallises out, the phenol is dissolved out by agitation with warm caustic soda, and separated by fractional neutralisation with sulphuric acid.

Tarry matter and compounds homologous with phenol are first precipitated, and finally the oily phenol itself. The crude phenol is purified by redistillation and fractional crystallisation; the oily mother liquors constitute the inferior forms of commercial carbolic acid.

*Phenol* or *carbolic acid*,  $C_6H_5.OH$  (Runge, 1834), is a colourless, crystalline substance, which melts at  $43^{\circ}$ , and boils at  $181^{\circ}$ ; on exposure to air and daylight, especially when not quite pure, it slowly reddens and deliquesces. Phenol is very corrosive and poisonous, and a powerful antiseptic; when pure its odour is aromatic and pleasant, and its taste sweet, but burning. It is fairly soluble in water, and freely in organic solvents, and is volatile with steam.

Phenol is slightly acid, and hence was originally termed carbolic or phenic acid, but its acid properties are so extremely feeble ( $K = 0.00000013$ ), that it does not interact with alkali carbonates; the alkali *phenates* or *phenoxides*, which are stable, crystalline compounds, formed by evaporating phenol with caustic alkalies, are decomposed by carbon dioxide, and afford a means of separating phenol from organic acids. Similarly the violet *ferric compound* is decolorised even by acetic acid.

On the other hand, phenol shows some of the properties of an alcohol, and has on this account been termed phenyl hydrate, or phenyl alcohol (Laurent, 1841; *phœneur*, to give light).<sup>\*</sup> When heated with acetic anhydride and sodium acetate it is converted into *phenyl acetate*,  $C_6H_5.OAc$ , a liquid which boils at  $195^\circ$ , and is hydrolysable in the normal manner to phenol and acetic acid. *Phenyl potassium sulphate*,  $C_6H_5.KSO_4$ , is formed by boiling a solution of potassium phenate with potassium pyrosulphate, and is excreted in the urine after the administration of phenol; it is a crystalline solid, which is stable towards alkalis.

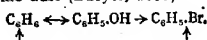
On heating sodium phenate with methyl iodide, phenyl methyl ether is formed; the action proceeds much more readily than with aliphatic compounds, and in presence of water.

*Phenyl methyl ether* or *anisole*,  $C_6H_5.O.CH_3$  (Carius, 1851), is a light, insoluble liquid, which boils at  $154^\circ$ , and has a very fragrant odour; *phenyl ethyl ether* or *phenetole*,  $C_6H_5.OEt$ , is a similar liquid boiling at  $172^\circ$ . These ethers are quite stable towards caustic alkalis, and are therefore not true ethereal salts; but unlike the aliphatic ethers they are hydrolysed by concentrated hydriodic acid at the ordinary boiling temperature (see also § 400).

*Phenyl ether*,  $(C_6H_5)_2O$ , a crystalline compound which is formed by fusing phenol with zinc chloride, is also quite stable; it cannot be made by methods analogous to those used in the preparation of ether, and is not decomposed by hydriodic acid.

The presence of hydroxyl, suggested by the acid and alcoholic properties of phenol, is confirmed in the usual manner, by the action of the phosphorus haloids. Hydrogen chloride and hydrogen bromide have no action upon it, but when it is heated with phosphorus pentabromide the hydroxyl is replaced by bromine; and as the phenyl bromide thus formed is identical with bromobenzene (Riche, 1862), phenol itself is *hydroxybenzene*.

This is confirmed by various syntheses, by the direct oxidation of benzene to phenol when shaken with hydrogen peroxide and ferrous sulphate, and by the direct conversion of phenol into benzene when its vapour is passed over red-hot zinc dust (Baeyer, 1866).



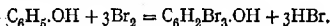
Considered as an alcohol, phenol resembles the tertiary alcohols, for when strongly oxidised it does not yield an acid or ketone containing the same number of carbon atoms, but simply breaks up; carbon dioxide is

<sup>\*</sup> From its occurrence in coal-gas bye-products; similarly the word *carbolic* is derived from *oleum carbonis*.



the principal product with concentrated permanganate at a high temperature.

As a benzene derivative phenol forms substitution products with the usual agents, namely halogens, nitric acid and sulphuric acid \*; when bromine water is added to a solution of phenol, tribromophenol is precipitated in light, white flocks, which may be recrystallised from alcohol.

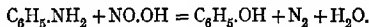


*Tribromophenol*,  $\text{C}_6\text{H}_2\text{Br}_3\text{.OH}$  (Laurent, 1842), is a crystalline substance, which melts at  $92^\circ$ , and has a very characteristic odour; it is readily reconverted into phenol by reduction with sodium amalgam and water.

The introduction of halogen into the benzene nucleus markedly increases the acidity of phenol, as might be expected; the dissociation constant of orthochlorophenol is  $K = 0.000004$ .

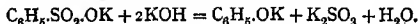
Besides the violet coloration with ferric chloride, phenol gives a characteristic colour reaction with nitrosulphonic acid; a colour changing from brown through green to an intense blue being obtained, on adding phenol to a solution of sodium nitrite in a large excess of concentrated sulphuric acid (Liebermann's reaction).

**255. Conversion of Benzene into Phenol.**—Aniline is readily converted into phenol by the action of nitrous acid; the operation is conducted in the same way as in the parallel conversion of ethylamine into alcohol (§ 58), the amino-group being replaced by hydroxyl (Hunt, 1859; compare § 258).



Cold sodium nitrite solution is added to an ice-cold solution of the base in dilute sulphuric acid, until a slight excess of nitrous acid is present; this is detected by means of test-papers, which have previously been soaked in potassium-iodide-starch solution and dried. The product is then heated on a water-bath for half an hour, and after the evolution of nitrogen has ceased the phenol is distilled with steam.

A second important synthesis consists in fusing potassium benzenesulphonate with caustic potash, the melting point of which has been lowered by adding a small quantity of water; the sulphonic radical is detached as alkali sulphite (compare § 247), and the phenyl radical is converted hydrolytically into potassium phenoxide (Kekulé, Wurtz, 1867).

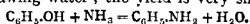


The alkali is melted in an iron or nickel dish with a little water, and

\* The nitrophenols and phenolsulphonic acids are considered later (§§ 294, 295).

the powdered sulphonate slowly stirred in. The mass is kept fused for half an hour at a temperature not exceeding  $300^{\circ}$ , and is then cooled and dissolved in water. On acidifying the filtered solution with dilute sulphuric acid, sulphur dioxide is given off in abundance, and, after the remainder has been expelled by boiling, the phenol can be extracted with ether. The yield with caustic soda is not nearly as good (§ 305).

Conversely, phenol can be converted into aniline by heating with solid ammonio-zinc chloride, at a high temperature. This double salt, which is formed by passing dry ammonia over zinc chloride, is dissociated by heat, and the zinc chloride thus set free assists the action of the ammonia in withdrawing water; the yield is very small, however.



**256. The Phenyl Radical: Aryl Radicals.**—The mono-substitution products of benzene are thus intermediate to the derivatives of the aliphatic acids and alcohols; the phenyl radical,  $\text{C}_6\text{H}_5$  or Ph, which passes through the various interactions, resembles on the one hand the tertiary alkyl radicals, and on the other hand, to a certain extent, the radicals of very feeble acids.

Phenol or phenyl hydroxidé is intermediate to the alcohols and acids, just as aniline or phenylamine is intermediate to the amines and amides. Radicals of the phenyl or aromatic class are termed generically aryl radicals.

The phenyl radical enters into combination with metals and other elements in the same way as the alkyl radicals. *Mercury diphenyl*,  $\text{Hg}(\text{C}_6\text{H}_5)_2$ , a crystalline substance melting at  $120^{\circ}$ , is thus formed by the action of sodium amalgam on a boiling solution of bromobenzene in benzene. *Phenyl isocyanide*,  $\text{C}_6\text{H}_5\text{N}:\text{C}$  (§§ 73, 249), is an unstable colourless oil, which boils at  $165^{\circ}$ , and resembles the alkyl isocyanides in odour; when pure, it rapidly turns blue and polymerises to a resin, but it may be kept unchanged if mixed with dry aniline or ether.

Phenyl mustard-oil (isothiocyanate, § 210) is formed by the interaction of carbon disulphide and mercuric chloride with aniline, or by boiling thiocarbamide with excess of concentrated hydrochloric acid; it separates as an oil, which can be distilled off with steam. *Phenyl isothiocyanate*,  $\text{C}_6\text{H}_5\text{N}:\text{CS}$ , is a colourless liquid, which boils at  $222^{\circ}$ , and has the pungent and characteristic odour of the mustard oils.

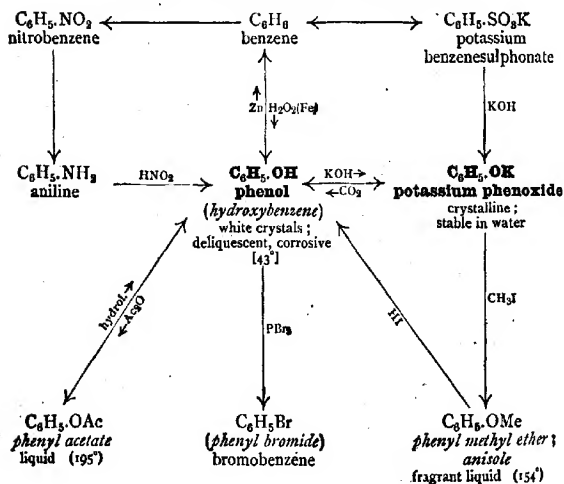
Phosphorus and sulphur compounds, analogous to aniline and phenol, are also known. The phenyl mercaptan, formed by reducing benzenesulphonic chloride (§ 247), is also made by fusing potassium benzenesulphonate with potassium hydrosulphide; and also from phenol itself by the action of phosphorus pentasulphide. *Phenyl mercaptan* or *thiophenol*,  $\text{C}_6\text{H}_5\text{SH}$ , is a mobile liquid, which boils at  $168^{\circ}$ ; its vapour is very irritating to the eyes.

Owing to the unique character of the phenyl radical, and in particular the fixity of the halogen in its halogen derivatives, the phenyl compounds are usually regarded simply as substitution products of benzene; aniline is considered as

*aminobenzene* (Griess), and not as phenylamine. We shall see later that there are other aromatic ammonia and hydroxy-derivatives, which much more closely resemble the aliphatic amines and alcohols (§§ 281, 280).

**257. Synopsis.**—Phenol is the hydroxy-compound corresponding with bromobenzene, and owing to the slightly acid character of the aryl radical, phenyl, it is intermediate in character to the aliphatic tertiary alcohols and the feeblar acids.

#### PHENOL AND THE PHENYL RADICAL.

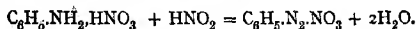


## CHAPTER XLVI

### DIAZONIUM AND RELATED COMPOUNDS

**258. Benzenediazonium Salts.**—In the conversion of aniline into phenol by nitrous acid, it is observed that phenol is not formed, or nitrogen evolved, until the product is warmed. The action occurs virtually in two stages, in the first of which the nitrogen forms a compound akin to the aliphatic diazo-esters (§ 219); and by working at a low temperature this intermediate diazonium compound can be isolated (Griess, 1858).

When nitrogen trioxide is passed into an ice-cold paste of aniline nitrate and water, a dark-brown liquid is obtained, from which, if the temperature has been kept low, a copious crystalline precipitate of benzenediazonium nitrate is thrown down on adding ice-cold alcohol-ether. When this is drained at the pump (Fig. 9, § 25) and washed with the same mixture, it forms a white silky mass, which must on no account be allowed to become dry, as it then detonates with great violence when rubbed or heated.

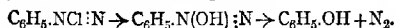


The corresponding sulphate is less dangerous; it is made by adding amyl nitrite (§ 230) slowly and with much stirring to a cold alcoholic solution of aniline sulphate; if crystals do not appear, a few drops of ether are added. The crystalline mass is drained at the pump, and washed successively with alcohol and ether; a second crop may be obtained by mixing the mother-liquor with the washings. The diazonium chloride is made in a similar manner, but the reagents must be well-cooled with ice (Knoevenagel, 1890).

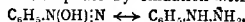
*Benzenediazonium nitrate*,  $\text{C}_6\text{H}_5\text{N}(\text{NO}_2):\text{N}$  (Griess, 1866), is an exceedingly explosive substance, which crystallises in silky needles. The *sulphate*,  $(\text{C}_6\text{H}_5\text{N}_2)_2\text{SO}_4$ , and *chloride*,  $\text{C}_6\text{H}_5\text{NCl}:\text{N}$ , are similar colourless salts; they are not so unstable as the nitrate, but explode when heated, and cannot be kept. These diazonium salts are derived from a complex ammonium base, benzenediazonium hydroxide.

The diazonium salts are very soluble in water, forming highly ionised solutions resembling those of the ammonium salts, their analogy to which is confirmed by the conversion of the chloride into a sparingly soluble, yellow *platinichloride*,  $(C_6H_5.N_2.Cl)_2.PtCl_4$ , and an insoluble, golden-yellow *aurichloride*,  $C_6H_5.N_2.Cl.AuCl_3$ . Moreover, the hydrochloride is decomposed by silver oxide in exactly the same way as the quaternary ammonium iodides (§ 214), the solution becoming strongly alkaline from the formation of an ammonium hydroxide. *Benzenediazonium hydroxide*  $C_6H_5.N(OH):N$ , is a highly ionised alkali, which is neutralised and reconverted into diazonium salts by acids.

When a solution of a benzenediazonium salt is heated it effervesces, and the whole of the nitrogen is liberated in the free state, whilst the phenyl radical is converted into phenol; the mechanism of the interaction of sodium nitrite with aniline hydrochloride is thus explained.

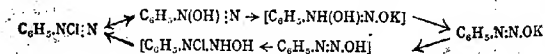


The diazonium compounds are thus mono-substituted derivatives of benzene. The linkage of the second nitrogen atom to the nitrogen of the aniline nucleus is confirmed by the conversion of these compounds into salts of phenylhydrazine,  $C_6H_5.NH.NH_2$  (§ 261), when reduced with zinc dust or other agents, and the reconversion of phenylhydrazine sulphate into the diazonium sulphate by oxidation with mercuric oxide.



**250. The Diazotates; Nitrosamines and Nitramines.**—Benzene-diazonium hydroxide is unstable in presence of alkalis, and neutralises them, although itself a powerful base; this apparent paradox is due to the conversion of the hydroxide into an isomeric acid, benzene-diazotic acid, the potassium salt of which is formed by adding the diazonium chloride to excess of cold, concentrated potash.

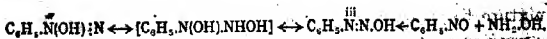
*Potassium benzenediazotate*,  $C_6H_5.N:N.OK$ , forms colourless silky needles; *benzenediazotic acid*,  $C_6H_5.N:N.OH$ , is not known in the free state, as it neutralises acids, owing to reconversion into the diazonium salt. When, however, the potassium salt is added to 50 per cent. acetic acid at  $-20^\circ$ , the acid anhydride is obtained; *benzenediazoxide*,  $(C_6H_5.N_2)_2O$ , is a yellow, insoluble substance, which is exceedingly dangerous, as it explodes spontaneously at  $0^\circ$ ; it is converted into a diazonium salt by strong acids, and is reconverted into the diazotate by potash.



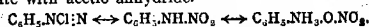
When the diazonium chloride is added to concentrated potash which is then heated quickly to  $140^\circ$ , a stereoisomeric potassium salt is obtained. *Potassium benzene-isodiazotate*,  $C_6H_5.N:N.OK$ , resembles the normal salt, but is more highly ionised and stable; the corresponding *isodiazotic acid* is transiently liberated by acids from the potassium salt, but is rapidly transformed into the diazonium compound.

With carbon dioxide, on the other hand, potassium isodiazotate yields the isomeric nitrosamine. *Phenylnitrosamine*,  $C_6H_5.NH.NO$ , (Hantzsch, 1902), is a yellow, crystalline substance, which is a pseudo-acid,





When benzenediazonium chloride is subjected to prolonged oxidation with cold alkaline potassium ferricyanide, the nitro-compound corresponding with phenyl-nitrosamine is formed; it is more readily obtained by the action of nitric anhydride on aniline in ether, or by dehydrating aniline nitrate with acetic anhydride.

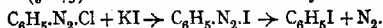


**Phenylnitramine**,  $\text{C}_6\text{H}_5\text{NH.NO}_2$  (Bamberger, 1895), is a colourless crystalline substance melting at  $46^\circ$ ; it is reduced to phenylhydrazine by sodium amalgam, but to benzene-diazonium salts by less energetic agents, and it is hydrolysed to aniline and nitric acid by alkalies at a high temperature. Phenylnitramine is converted by strong acids into the isomeric nitranilines (§ 293); like the nitroparaffins it forms metallic salts derived from a labile isomeride, namely *benzenediazoic acid*.

**Sodium benzenediazoate**,  $\text{C}_6\text{H}_5\text{N:NO.ONa}$ , like the sodium diazotates, yields an *N*-ether with methyl iodide, whilst the *silver salt* yields an *O*-ether. **Phenylmethylnitramine**,  $\text{C}_6\text{H}_5\text{NMe.NO}_2$ , the *N*-ether, is a crystalline substance melting at  $39^\circ$ , which is converted by acids into the isomeric nitrotoluidines (§ 293); **methyl diazoate**,  $\text{C}_6\text{H}_5\text{N:NO.OMe}$ , the *O*-ether, is an explosive oil which yields methyl alcohol when hydrolysed.

**260. The Diazonium Interactions.**—The diazonium compounds are useful by reason of their very instability. Besides the hydrolytic conversion of aniline into phenol, due to their successive formation and decomposition, various other decompositions can be effected, by means of which the phenyl radical may be brought into combination with halogen, etc.

On warming a solution of potassium iodide to which a diazonium salt has been added, nitrogen is evolved, but the phenyl radical now unites mainly with the iodine ions, and iodobenzene (§ 245) is thrown down as a heavy oil.

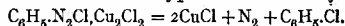


Similar results are obtained with hydrochloric and hydrobromic acids, although much more phenol is now formed. The action is rendered almost quantitative, however, by substituting the cuprous salt for the acid, or more simply by adding precipitated copper to the mixture; it is then unnecessary to isolate the diazonium salt.

A concentrated solution of sodium nitrite is added to the well-cooled solution of the aniline salt, until a permanent excess of nitrous acid is shown by iodide-starch paper (the condensation to the diazonium salt is slow, and hence there is a temporary excess of the acid after each addition of nitrite); the amine thus diazotised is then added to the solution containing the required radical, and after warming the

mixture to complete the action, the product is isolated by extraction with ether, or otherwise.

Chlorobenzene and iodobenzene are much more readily prepared by this method than by direct substitution; its great value, however, lies in its universal applicability, for practically any compound of the aniline type can be similarly dealt with.



If a diazotised solution of aniline be added slowly to a boiling solution of cuprous chloride in hydrochloric acid (Sandmeyer, 1884) or precipitated copper be added to a mixture of the diazotised solution with excess of hydrochloric acid, at the ordinary temperature (Gattermann, 1890), chlorobenzene is formed quantitatively. Bromobenzene may be prepared in a similar manner from benzene-diazonium sulphate, potassium bromide and reduced copper.

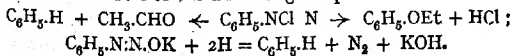
The accelerating effect of cuprous copper is due to the formation of double cuprous salts analogous to potassium cuprochloride; *diazonium cuprochloride*,  $\text{C}_6\text{H}_5\cdot\text{N}_2\cdot\text{Cl}\cdot\text{Cu}_2\text{Cl}_2$ , is a yellow substance which is resolved into cuprous chloride, nitrogen and chlorobenzene, when heated with water; it can be seen transiently as the diazotised solution meets the cuprous solution; the cuprous chloride by combining with the diazonium chloride prevents its decomposition into phenol.

A very important variant of the diazonium-halogen interaction is the synthesis of nitriles from amines by replacing the amino-group by cyanogen. When a cold diazotised solution of aniline hydrochloride is poured slowly down the condenser of a reflux apparatus, which contains a hot solution of potassium cuprocyanide (§ 201), cyanobenzene (benzonitrile, § 267), is formed, with excellent yield; the process is exactly parallel to the formation of chlorobenzene, and the product is purified in the same way.



Other radicals may be introduced into the benzene nucleus in the same manner. One of the most important of these changes is the replacement of the amino-group by hydrogen, by which process the amine is reconverted into the compound from which the antecedent nitro-derivative was obtained.

The exchange is effected in some cases by boiling the diazonium salt with alcohol (Griess, 1866), but as the main product of this interaction is usually a phenolic ether (Remsen, 1886), it is better to reduce the corresponding diazotate with an alkaline stannite. The operation is termed the elimination of the amino-group.

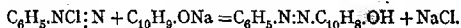


The stannite solution is prepared by adding caustic soda to cooled stannous chloride solution, until the stannous hydroxide has redissolved: the diazonium solution is converted into diazotate, by pouring into well-

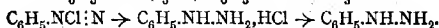
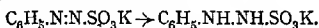


cooled concentrated caustic soda, and the diazotate is added slowly to the alkaline stannite through the condenser of a reflux apparatus. Nitrogen is evolved in abundance, and benzene rises to the surface (Friedländer, 1889); it can either be distilled off with steam, or separated mechanically.

The diazonium compounds and diazotates are further characterised by the ease with which they interact with benzenoid amines and phenols, forming highly-coloured azo-compounds (§ 382). The interaction with  $\beta$ -naphthol (§§ 371, 383) is particularly smooth, a brilliant red precipitate being rapidly formed on addition of a diazonium salt or diazotate to an alkaline solution of this substance.



**261. Phenylhydrazine.**—The reagent phenyl-hydrazine is formed by reducing diazonium salts in neutral or acid solution by means of alkali sulphites (with or without zinc and acetic acid), or stannous chloride.



On adding diazotised aniline hydrochloride to a concentrated ice-cold solution of sodium sulphite, the product becomes almost solid with a yellow crystalline compound, *sodium benzenediazosulphonate*,  $\text{C}_6\text{H}_5\cdot\text{N}:\text{N}\cdot\text{SO}_3\text{Na}$ , which is reduced to the corresponding *phenylhydrazinesulphonate*,  $\text{C}_6\text{H}_5\cdot\text{NH}\cdot\text{NH}\cdot\text{SO}_3\text{Na}$ , by warming either with more sodium sulphite, or with zinc dust and acetic acid. On hydrolysing the filtered and concentrated solution of the sulphonate by boiling with concentrated hydrochloric acid, the compound is resolved into phenylhydrazine and sulphuric acid; the hydrochloride of the base crystallises out as the solution cools (Fischer, 1878).

A similar result is obtained somewhat more quickly by means of stannous chloride. A well-cooled solution of stannous chloride in concentrated hydrochloric acid is added to aniline hydrochloride, which has been ground up with a large volume of the same acid, and diazotised in the usual manner; the crystalline phenylhydrazine hydrochloride, which rapidly separates, is collected and drained (Victor Meyer, 1883).

The hydrazine hydrochloride obtained by either method is dissolved in a little water, and the base liberated with caustic soda, and extracted with ether; after drying with anhydrous potassium carbonate and distilling off the ether (§ 249), the free hydrazine is fractionated under reduced pressure.

*Phenylhydrazine*,  $\text{C}_6\text{H}_5\cdot\text{NH}\cdot\text{NH}_2$  (Fischer, 1878), is a colourless crystalline solid, having a pleasant aromatic odour; it melts at  $23^\circ$ , and boils at  $242^\circ$ , but decomposes slightly at the latter temperature. Like aniline, it is slowly oxidised by the air, turning brown and syrupy.

*Phenylhydrazine hydrochloride* is a stable crystalline salt; the *acetate*, which is less stable, may be made by adding excess of sodium acetate and a little acetic acid to the aqueous solution of the hydrochloride; or by dissolving the base in dilute acetic acid, and filtering from any resinous impurity.

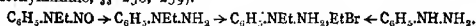
Phenylhydrazine is a moderately powerful reducing agent. When it is boiled with alkaline copper tartrate, cuprous oxide is precipitated, whilst with acetic acid and copper sulphate solution, nitrogen is eliminated, and benzene set free; the action is quantitative. Under the same conditions, phenylhydrazine hydrochloride is converted into chlorobenzene; but when distilled with zinc dust it is reduced to aniline and ammonia.



As an aminoid compound, the hydrazine forms additive salts with acids. With alkyl iodides and nitrous acid, it behaves as a secondary amine; *phenyl-nitrosohydrazine*,  $\text{C}_6\text{H}_5\cdot\text{N}(\text{NO})\cdot\text{NH}_2$ , is an unstable substance, which is quickly dehydrated to phenylazoimide (§ 265).

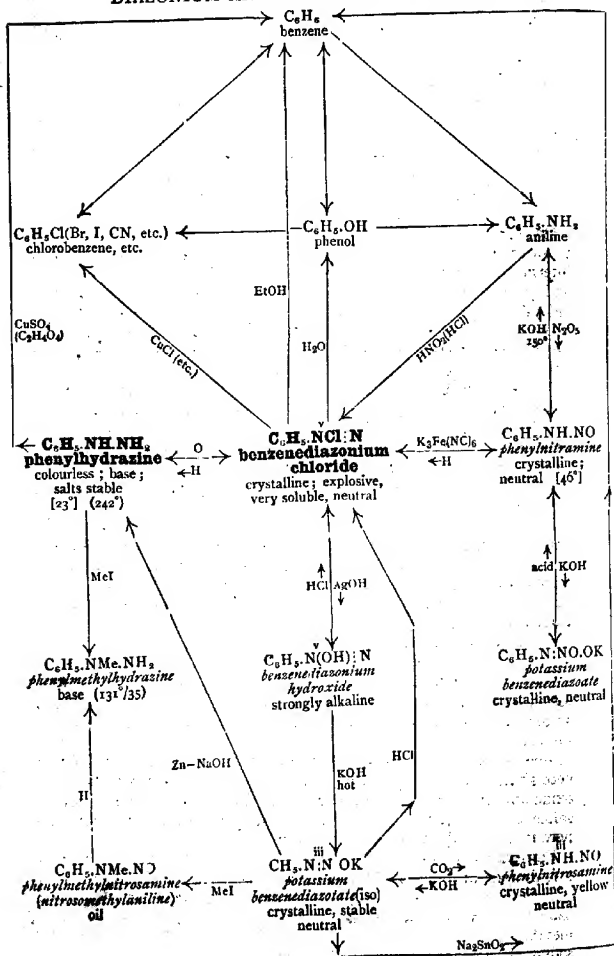
Phenylhydrazine is a valuable reagent for aldehydes and ketones, with which, in acetic acid solution, it forms condensation products, the *hydrazones* (Fischer, 1884, §§ 85, 89), which are readily hydrolysed by mineral acids. The *osazones* or double hydrazones (§ 185), and the *hydrazides* or hydrazine amides (§ 181) have also been dealt with previously.

The constitution of phenylhydrazine follows in part from its interconvertibility with aniline, and in part from its relation to ethylaniline. By reducing the nitroso-compound of this secondary amine, *ethyl-phenylhydrazine* is formed, and this base combines with ethyl bromide to form an additive compound, *ethyl-phenylhydrazine ethobromide*, which is identical with that which results from the action of ethyl bromide on phenylhydrazine itself (Fischer, 1878; compare Phenylmethylnitrosamine or nitrosomethylaniline, §§ 250, 259).



**262. Synopsis.**—Aniline differs from the aliphatic amines in that it forms with nitrous acid a condensation product, benzenediazonium hydroxide, by means of which it is convertible not only into the corresponding hydroxy-compound, phenol, but also into the hydrocarbon, and its halogen and cyanoderivatives, and into a derivative of hydrazine.

## DIAZONIUM AND RELATED COMPOUNDS.



## CHAPTER XLVII

### NITROBENZENE AND ALLIED COMPOUNDS

**265. Nitrosobenzene and Phenylhydroxylamine.**—The reduction of nitrobenzene to aniline is not the simple process it at first sight appears to be ; several intermediate products are known, the simplest of which are nitrosobenzene and phenylhydroxylamine. When the oxidation of benzenediazonium chloride to phenylnitramine by alkaline ferricyanide (§ 259) is interrupted, the product is found to contain nitrosobenzene, which may also be obtained directly from aniline, by oxidation with alkaline permanganate.

The same compound is formed by the prolonged action of ice-cold caustic alkalis on *benzene-diazonium perbromide*,  $C_6H_5.N_2Br_3$ , a crystallisable oil, which is precipitated by adding a diazotised aniline solution to bromine dissolved in potassium bromide. It is most readily obtained by oxidising phenylhydroxylamine sulphate with dilute chromic acid at  $0^\circ$ , and is isolated by distillation with steam, with which it is extremely volatile.

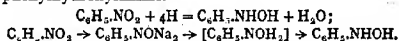
*Nitrosobenzene*,  $C_6H_5.NO$  (Baeyer, 1875), is a colourless, crystalline substance, which melts at  $68^\circ$  to an emerald green liquid (compare Nitrosomesitylene, § 328), and has a pungent odour resembling that of the carbimides. It readily condenses with aniline in hot glacial acetic acid, forming azobenzene (§ 380), and with hydroxylamine, forming isodiazotic acid (§ 259); and it is converted into nitrobenzene by oxidation with alkaline hydrogen peroxide.



Phenylhydroxylamine is readily prepared by cautiously reducing nitrobenzene in neutral solution, preferably with zinc, in which case ammonium chloride or calcium chloride must be present to combine with the zinc oxide. On adding zinc-dust slowly to an emulsion of the nitro-compound in dilute ammonium chloride, there is an energetic action, necessitating the cooling of the liquid; when this has ceased, the zinc oxide and excess of metal are filtered off, and the phenylhydroxylamine salted out with common salt. The crystals are then drained, dried on a porous plate, and recrystallised from benzene.

Phenylhydroxylamine is also formed from aniline by oxidation with persulphuric acid, and is further produced from the sodium derivative of nitrobenzene. Nitrobenzene, like the aliphatic tertiary nitro-compounds, cannot assume a labile acidic form (§ 232), and hence does not form metallic compounds of the ordinary type; when, however, it is boiled with sodium in toluene, it exchanges oxygen for sodium, forming a *sodium compound*,  $C_6H_5.NONa_2$  (possibly  $C_6H_5.NNa.ONa$ ), which, when sus-

pended in ether and shaken with ammonium chloride solution, is hydrolysed to phenylhydroxylamine.



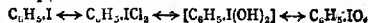
*Phenylhydroxylamine*,  $\text{C}_6\text{H}_5\cdot\text{NH}\cdot\text{OH}$  (Wohl, 1894), is a colourless, crystalline substance, which melts at  $81^\circ$ , and irritates the skin and mucous membrane; it can be kept in dry, air-tight vessels, but is unstable and rapidly changed by air, acids or alkalis. On account of its ready oxidability, it reduces alkaline copper and cold ammonio-silver solutions energetically; it is rapidly re-oxidised to nitrobenzene by the combined action of air and alkalis, whilst with dilute chromic acid nitrosobenzene is formed. By the action of air or alkalis alone, azoxybenzene (§ 380) is produced by condensation, whilst mineral acids effect an isomeric conversion into *p*-aminophenol (§ 294). With nitrous acid phenylhydroxylamine forms a crystalline *nitroso-compound*,  $\text{C}_6\text{H}_5\cdot\text{N}(\text{NO})\cdot\text{OH}$ , a sparingly soluble acid substance, which has but feeble reducing action, and is hydrolysed by warm acids to nitrosobenzene.

Both nitrosobenzene and phenylhydroxylamine are formed by the electrolytic reduction of nitrobenzene, and if the nitrobenzene is dissolved in concentrated sulphuric acid, a large yield of *p*-aminophenol sulphate is produced, by isomerisation of the phenylhydroxylamine.

**264. Iodosobenzene, Iodoxybenzene and Iodonium Bases.**—The many different functions of nitrogen in organic compounds are largely due to the ease with which its valency can be varied; we have repeatedly noticed that compounds which may be saturated and inert with regard to one set of reagents, may become unsaturated and mobile with regard to another set. A remarkable instance of such variable valency is found in the oxidation products of the comparatively inert substance, iodobenzene; the iodine becomes trivalent, and functions similarly to the nitrogen of the nitroso-, nitro- and ammonium compounds. The first compounds of this type were made from *o*-iodobenzoic acid (Victor Meyer, 1892).

Chlorine is rapidly absorbed by iodobenzene, just as by free iodine, and if the chlorination is carried out in ice-cold chloroform solution, a crystalline product is readily isolated. *Phenyl iodochloride*,  $\text{C}_6\text{H}_5\cdot\text{ICl}_2$  (Willgerodt, 1885), is a yellow, crystalline substance, which is in many respects analogous to the dichloramines,  $\text{R}\cdot\text{NCl}_2$ , although more stable. When heated it dissociates into iodobenzene and chlorine, whilst at the ordinary temperature it is gradually changed into *p*-chloriodobenzene,  $\text{Cl}\cdot\text{C}_6\text{H}_4\cdot\text{I}$ , and benzene; but when it is digested with cold caustic soda, it is slowly hydrolysed to the corresponding oxy-derivative, iodosobenzene, which is readily isolated, as it is insoluble in water.

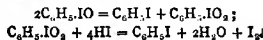
*Iodosobenzene*,  $\text{C}_6\text{H}_5\cdot\text{IO}$  (Willgerodt, 1892), is an unstable, yellow substance, analogous to nitrosobenzene in constitution; it has basic properties, however, and when evaporated with glacial acetic acid, forms a stable crystalline *acetate*,  $\text{C}_6\text{H}_5\cdot\text{I}(\text{OAc})_2$ , melting at  $157^\circ$ . Iodosobenzene rapidly and quantitatively liberates iodine from hydriodic acid, being itself reduced to iodobenzene; and it is reconverted into the iodochloride by phosphorus pentachloride.



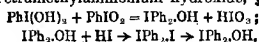
When iodosobenzene is heated in a water-bath, or distilled with steam, part is reduced to iodobenzene, but the remainder is oxidised to iodoxy-

benzene, a compound which is analogous to nitrobenzene in constitution the same product is obtained by directly oxidising phenyliodochloride with hypochlorites or persulphuric acid.

*Iodoxybenzene*,  $C_6H_5.IO_2$ , is a stable compound, which can be crystallised from water, but decomposes with a slight explosion when heated; like the iodoso-compounds it quantitatively oxidises hydriodic acid, being itself reduced to iodobenzene.

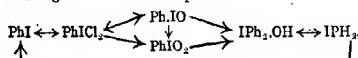


By the interaction of iodoso- and iodoxybenzene a basic iodonium compound is formed, which is analogous to the ammonium hydroxides. It is conveniently isolated by saturating with sulphur dioxide the alkaline mother-liquor from the iodoso-benzene preparation; part of the iodoso-compound is oxidised to the iodoxy-compound by air during the slow hydrolysis, and the sulphurous acid reduces the accompanying iodic acid to hydriodic acid, with which the base forms a sparingly soluble iodide; the free base is obtained by the action of silver oxide and water on the iodide (compare Tetramethylammonium hydroxide, § 214).

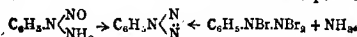


*Diphenyliodonium hydroxide*,  $(C_6H_5)_2I.OH$  (Victor Meyer, 1894), is a caustic, alkaline syrup, which absorbs carbon dioxide and neutralises acids, forming stable crystalline salts. The *nitrate*,  $IPH_2.NO_3$ , which can be crystallised from hot water, melts at  $154^\circ$ ; the *sulphate* and *acetate* are similar; the *iodide*,  $IPH_2.I$ , a pale yellow crystalline substance melting at  $176^\circ$ , is polymeric with iodobenzene, into which it is suddenly decomposed when heated.

The diphenyliodonium radical behaves in some respects like a heavy metallic radical; the *sulphide*,  $(IPH_2)_2S_3$ , formed by the action of yellow ammonium sulphide on soluble iodonium salts, is an orange-red precipitate resembling antimonious sulphide.

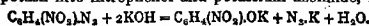


**26b. Phenylazotimide: Hydrazine and Azotimide.**—The dehydration product which is formed by warming phenyl-nitrosohydrazine with water, is also produced by the action of ammonia on diazobenzene perbromide.



*Phenylazotimide*,  $C_6H_5.N_3$  (Griess, 1867), the constitution of which follows from these methods of formation, is a yellow insoluble oil, of very penetrating and unpleasant odour; when heated under ordinary pressure it explodes, but it can be distilled unchanged under very low pressure.

Phenylazotimide is the phenyl derivative of *hydrazoic acid* or *azotimide*,  $N_3H$ . Like the halogen benzenes it cannot itself be hydrolysed, but its nitro-derivative, prepared from nitraniline (§ 293), is readily resolved by boiling potash into nitrophenol and potassium azotimide,  $N_3K$ .



Azotimide can itself be made in this way from guanidine. The *amino-guanidine hydrochloride* formed by reducing nitroguanidine,  $NH_2.C(NH).NH_2.NO_2$  (§ 227), is diazotisable in the same way as aniline, and the *guani-*

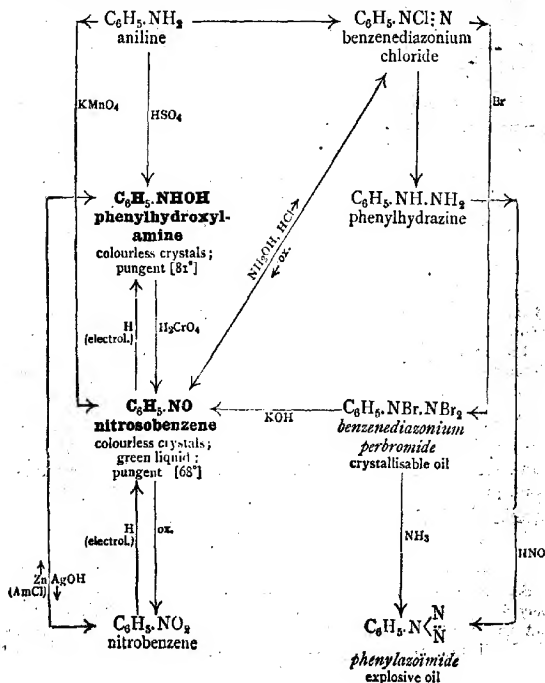
dine-diazonium chloride, thus formed, is resolved by caustic soda into cyanamide and sodium azoimide, from which azoimide gas is set free by acids.



Free hydrazine can also be made from aminoacetic acid by the diazonium reaction, ethyl diazoacetate being reduced and hydrolysed in much the same way as the guanidine-diazonium compound (Curtius, 1887).

**266. Synopsis.**—Nitrosobenzene and phenylhydroxylamine are intermediate compounds in the reduction of nitrobenzene to aniline. Iodosobenzene is an analogous compound in which the nitrogen is replaced by tervalent iodine; the ternary iodonium bases are similarly analogous to the quaternary ammonium bases.

#### NITROSOBENZENE AND PHENYLHYDROXYLAMINE.



## SECTION XII

### THE BENZYL-BENZOIC GROUP

#### CHAPTER XLVIII

##### BENZOIC ACID : THE BENZOYL RADICAL

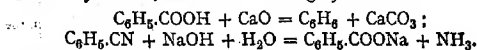
**287. Benzoic Acid.**—The acid from which benzene derives its name, is a volatile substance which occurs free in gum benzoin, and sublimes on gently heating this natural product (16th century); it is a typical aromatic acid.

*Benzoic* or *benzene-carboxylic acid*,  $C_6H_5.COOH$ , is a feathery crystalline substance, which melts at  $121^\circ$ , and boils at  $249^\circ$ , but sublimes readily far below its boiling point; it is also volatile with steam. The vapour is characteristically aromatic in odour, but irritating to the throat, causing persistent coughing; it burns with a luminous and smoky flame.

The acid is more economically extracted from the gum by boiling it with milk of lime, and decomposing the resulting calcium benzoate with hydrochloric acid (Scheele); it is manufactured by heating calcium phthalate (§ 324) with slaked lime at a moderate temperature, or by hydrolysing or hydrolytically oxidising the chlorination-products of toluene (§ 280).

The dissociation constant of benzoic acid is  $K=0.0060$ , so that it is decidedly stronger than the fatty acids; the aryl radicals are more negative in character than the alkyl radicals (§§ 249, 254).

When distilled with lime, benzoic acid is resolved into carbon dioxide and benzene, to which it therefore bears the same relation as acetic acid to methane. This relationship is confirmed by its preparation from the hydrocarbon by the cyanide synthesis, benzonitrile being cyanobenzene.

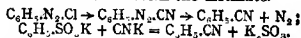


Benzonitrile can be prepared synthetically from the hydrocarbon, not only through aniline by the diazonium method (Sandmeyer, 1884, § 260), but also through benzenesulphonic acid; the alkali salt of this acid is simply distilled with dry potassium cyanide or anhydrous potassium



ferricyanide (Merz, 1868), the decomposition being parallel to that which occurs in the preparation of phenol from benzenesulphonic acid (§ 255).

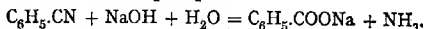
In either case the product is purified by distillation with steam, the pure nitrile being extracted with ether from the distillate.



Benzonitrile can also be made by distilling benzoic acid with potassium or lead thiocyanate (Letts, 1372), or dehydrating benzamide with phosphorus pentoxide; it was originally obtained by distilling dry ammonium benzoate.

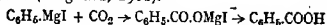
*Benzonitrile* or *phenyl cyanide*,  $\text{C}_6\text{H}_5\cdot\text{CN}$  (Fehling, 1844), is a colourless liquid, which resembles oil of bitter almonds (§ 275) in odour, and boils at  $191^\circ$ ; it was the first simple nitrile prepared, and furnished the name for the class.\*

When this nitrile is boiled with caustic alkali, ammonia is evolved in the normal manner, and on acidifying the alkaline residue benzoic acid is precipitated.



The same result may be obtained more directly by heating the nitrile with moderately concentrated sulphuric acid, and diluting the product. The acid is purified by repeated precipitation by hydrochloric acid from alkaline solution, and finally by sublimation through filter paper between watch-glasses.

Benzoic acid can also be synthesised by passing carbon dioxide into a solution of magnesium phenyl iodide, made by dissolving magnesium turnings in an ethereal solution of iodobenzene; the oily product is hydrolysed by water to magnesium benzoate, from which the acid is readily obtained as above (Grignard, 1901).



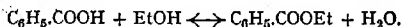
Synthetic benzoic acid is in every respect identical with the natural product, and with that prepared from the natural products benzaldehyde (§ 275) and hippuric acid (§ 271).

**268. Acid Derivatives of Benzole Acid: the Benzoyl Radical.**—Benzoic acid resembles acetic acid in most of its actions. Its alkali salts, such as *potassium benzoate*,  $\text{C}_6\text{H}_5\cdot\text{COOK}$ , are crystalline and soluble; the *silver salt*,  $\text{C}_6\text{H}_5\cdot\text{COOAg}$ , crystallises well and is anhydrous; the *ferric salt*,  $\text{Fe}(\text{O}\cdot\text{CO}\cdot\text{C}_6\text{H}_5)_3$ , is a buff, pulverulent precipitate, which like ferric acetate is at once hydrolysed by hydrochloric acid.

The benzoic esters resemble those of acetic acid, and may be made in the same way. *Ethyl benzoate*,  $\text{C}_6\text{H}_5\cdot\text{COOEt}$ , a fragrant liquid boiling at  $213^\circ$ , is formed by the action of benzoyl chloride and caustic soda on alcohol (§ 270); it is conveniently prepared by boiling an alcoholic solution of the

\* The prefixes *nitro*- and *azo*- had already been appropriated.

acid containing hydrochloric or sulphuric acid, excess of which is detrimental.



The product is poured into water, the ester separating as a heavy layer, which is washed, dried and fractionated in the usual way; a further quantity may be obtained by extracting the washings with ether.

Like acetic acid, benzoic acid forms a chloride and an oxide. The former, which was the first acid chloride prepared, is made by the action of phosphorus pentachloride on the acid.



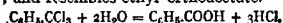
The two solids are shaken together until the mass is liquid, and hydrogen chloride ceases to be evolved, and the high-boiling benzoyl chloride is separated from the phosphorus oxychloride by simple fractionation. The chloride was originally made by direct chlorination of benzaldehyde and is still manufactured in this way.

*Benzoyl chloride*,  $\text{C}_6\text{H}_5\text{COCl}$  (Liebig, 1832), is a heavy, colourless liquid, having a pungent, oppressive, aromatic odour; it boils at  $198^\circ$ , freezes at  $-1^\circ$ , and has a specific gravity of 1.21 at  $20^\circ$ .

Like acetyl chloride, benzoyl chloride is hydrolysed by water, although much more slowly; it is unaffected by cold water, and only slowly by boiling water, but is dissolved by hot caustic soda. Similarly it interacts with alcohols and amines, forming benzoic esters and substituted benzamides (§ 270).

The oxide, benzoic anhydride, is formed in a similar manner to acetic anhydride, by boiling benzoyl chloride with sodium benzoate, and then distilling the chlorine-free product. *Benzoic anhydride*,  $(\text{C}_6\text{H}_5\text{CO})_2\text{O}$ , is a crystalline substance melting at  $42^\circ$ .

Whilst benzoyl chloride and benzoic anhydride are less easily hydrolysed than the corresponding acetyl compounds, their oxygen is more readily replaced by chlorine. *Benzotrichloride*,  $\text{C}_6\text{H}_5\text{CCl}_3$ , a liquid boiling at  $213^\circ$ , which is formed by the action of phosphorus pentachloride on either compound, is hydrolysed by boiling water to benzoic and hydrochloric acids (compare § 77). Similarly, when heated with alcoholic sodium ethoxide, it is converted into *ethyl orthobenzoate*,  $\text{C}_6\text{H}_5\text{C}(\text{OEt})_3$ , a liquid which boils at  $220^\circ$ , and resembles ethyl orthoacetate.



As regards those actions into which it enters as a carboxylic acid, benzoic acid is thus very similar to acetic acid. It is the hydroxide of an acidic or acyl radical benzoyl,  $\text{C}_6\text{H}_5\text{CO}$  or  $\text{Bz}$  (benzoic and  $\text{Bz}$ , Liebig and Wöhler), which was the first acid radical recognised.

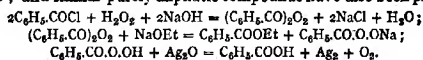
289. *Perbenzoic Acid*.—When benzoyl chloride is shaken with a concentrated solution of hydrogen peroxide, which has been rendered alkaline

with caustic soda, it is converted into *benzoyl peroxide*,  $(C_6H_5.CO)_2O_2$ ; this is a sparingly soluble crystalline compound, which melts at  $103^\circ$ , and then decomposes with a slight explosion. Benzoyl peroxide is converted by alcoholic sodium ethoxide into ethyl benzoate and *sodium perbenzoate*,  $C_6H_5.CO.O.Na$ , a white powder from which the free acid is liberated by dilute mineral acids; it is isolated by extraction with chloroform.

*Perbenzoic acid* or *benzoyl hydrogen-peroxide*,  $C_6H_5.CO.O.OH$  (Baeyer, 1900), is a crystalline substance which melts at  $43^\circ$ , and boils unstably at  $100^\circ/14$  mm.; unlike benzoyl peroxide, it has a strong, unpleasant odour resembling that of hypochlorous acid.

Perbenzoic acid is a powerful oxidising agent; it liberates iodine from potassium iodide, bleaches indigo solutions, and oxidises aniline to nitrosobenzene (§ 263); like hydrogen peroxide also, it reduces silver oxide, losing its peroxidic oxygen; it is similarly decomposed by manganese dioxide, and converts chromic acid into the unstable blue peroxide.

Benzoyl peroxide interacts with acetic anhydride, forming *acetyl benzoyl peroxide*; and similar purely aliphatic compounds have also been prepared.



**270. Benzoylation of Alcohols and Amines.**—On account of its comparative stability, and by reason also of the better definition and higher melting points of its derivatives, benzoyl chloride is often used instead of acetyl chloride as a test for alkylic and phenolic hydroxyl. A further advantage is that as the benzoyl compounds are usually at most sparingly soluble in cold water, the benzoylation, as it is termed, can be carried out in aqueous solution.

The benzoyl chloride is added to the cold solution of the substance, which is then made distinctly alkaline with caustic soda, shaken violently and gently warmed, the addition of alkali and shaking being repeated until the product remains permanently alkaline; the benzoylated product either crystallises on cooling, or separates as an oil which crystallises when rubbed (Schotten, Baumann, 1887).

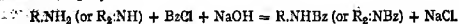
Ethyl benzoate is thus almost instantly prepared by warming an alcoholic solution of benzoyl chloride with caustic soda until permanently alkaline; it separates on adding water to the product.



Phenol may similarly be converted in aqueous solution into *phenyl benzoate*,  $C_6H_5.OBz$ , a crystalline substance melting at  $71^\circ$ . Glycerol gives *glyceryl tribenzoate* or *tribenzoyl glycerol*,  $C_6H_5(OBz)_3$ , melting at  $76^\circ$ ; mannitol is converted into *hexabenzoyl mannitol*,  $C_6H_5(OBz)_6$ , melting at  $132^\circ$ ; whilst from glucose, *pentabenzoyl glucose*,  $C_6H_5O(OBz)_5$ , melting at  $179^\circ$ , is obtained.

The procedure with aminoid compounds is similar, compounds such as

benzoylaniline or benzanilide (§ 271) and benzoylaminoacetic acid (hippuric acid, § 271) being readily formed. Instead of benzoyl chloride, phenylacetyl chloride (§ 282) and benzenesulphonic chloride (§ 247) are sometimes employed.



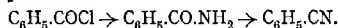
The process of benzoylation is sometimes more readily effected in alcoholic solution, in which case excess of sodium ethoxide is substituted for the caustic alkali, and shaking is unnecessary (Claisen).

**271. Benzamide and Hippuric Acid.**—Benzoyl chloride interacts with ammonium carbonate or ammonia in the same way as, but much more rapidly than, acetyl chloride, forming the corresponding amide, benzamide.

This compound is also formed synthetically by the interaction of benzene and chloroformamide in presence of aluminium chloride (§ 279), which is without analogy among the aliphatic compounds.



*Benzamide*,  $C_6H_5.CONH_2$  (Liebig, 1833), is a crystalline substance, which melts at  $130^\circ$ , and unlike the fatty amides is soluble only in boiling water. As an amide it is hydrolysed to ammonia and sodium benzoate by boiling caustic soda solution, and dehydrated to benzonitrile by distillation with phosphorus pentoxide.



Benzamide is converted by cold sodium hypobromite into the *bromamide*,  $C_6H_5.CO.NHBr$ , which may be isolated from the acidified solution; but if the alkaline product be warmed the bromamide is converted into aniline, by a process analogous to the conversion of acetobromamide into methylamine (§ 212).

Benzamide forms the usual unstable compounds with acids, but on account of the negative character of the phenyl radical its metallic derivatives are fairly stable. The alkyl derivatives occur in two modifications, derived respectively from benzamide and isobenzamide (compare Imino-chlorides, § 227); the imino-ether yields ammonia and alcohol when hydrolysed, whereas the ethylamide gives ethylamine.

Silver benzamide interacts with cold ethyl iodide forming *benziminio-ether*,  $C_6H_5.C(OEt).NH$ , an unstable liquid derived from isobenzamide; this is isomerised by heat, especially in presence of alkyl iodides, to the corresponding *N*-ether. *Benzethylamide*,  $C_6H_5.CO.NH.Et$ , the true benzamide derivative, is a crystalline substance which is identical with benzoylated ethylamine.

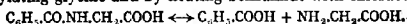
The corresponding phenylamide, benzanilide, is readily made by benzoylating aniline. *Benzanilide*,  $C_6H_5.CO.NH.C_6H_5$ , is a crystalline substance melting at  $165^\circ$ ; it is reconverted into benzoic acid and aniline when hydrolysed.

Benzoyl-glycine occurs in the urine of herbivorous animals, and is known as hippuric acid; it is readily obtained by

evaporating horses' or cows' urine to one-sixth, and purifying the crude acid which crystallises out by boiling with water and animal charcoal.

*Hippuric* or *benzoylaminoacetic acid*,  $C_6H_5.CO.NH.CH_2.CO.OH$  (Rouelle, 1773), is a colourless, crystalline substance, melting at  $187^\circ$ ; it is readily soluble in hot, but only sparingly in cold water, and is insoluble in light petroleum.

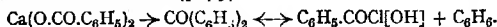
As an amide, hippuric acid is hydrolysed by boiling hydrochloric acid to benzoic acid and the complex ammonia, glycine, the benzoic acid crystallising out on cooling (Dessaignes, 1846); it may be synthesised both by benzoylating glycine and by heating benzamide with chloroacetic acid.



As a monobasic acid ( $K=0.022$ ), hippuric acid forms metallic and alkyl salts; the *ferric salt*, precipitated by ferric chloride from a neutral solution of a hippurate, is a brown flocculent precipitate, which is further distinguished from the corresponding benzoate by yielding ammonia when heated with soda-lime.

The corresponding *phenylaminoacetic acid* or *phenylglycine*,  $C_6H_5.NH.CH_2.CO.OH$ , a soluble crystalline substance melting at  $127^\circ$ , is similarly prepared by heating aniline with chloroacetic acid and sodium acetate; it has marked acid properties ( $K=0.0039$ ), and is of interest from its ready conversion into indigo and related compounds (§ 337).

**272. Benzophenone and Acetophenone: Transformation of Oximes into Anilides.**—Benzoic acid further resembles acetic acid in that it is converted into a ketone when its calcium salt is distilled; this ketone, however, is better prepared by the interaction of benzoyl chloride with benzene in presence of aluminium chloride (§ 279).



*Benzophenone* or *diphenylketone*,  $C_6H_5.CO.C_6H_5$ , is a fragrant crystalline substance, which melts at  $48^\circ$ , and boils stably at  $307^\circ$ .

As a ketone it forms a *hydrazone*, *oxime*, *semicarbazone*, etc., all well-defined crystalline substances; and it is reducible to a secondary alcohol, *benzhydrol*,  $C_6H_5.CHOH.C_6H_5$ , from which it is recovered by oxidation. When fused with caustic potash it is reconverted into benzoic acid and benzene.

A similar mixed ketone, acetophenone, is formed by distilling a mixture of calcium benzoate and acetate, or by the action of acetyl chloride on benzene in presence of aluminium chloride, as well as by the various methods used in the formation of aliphatic ketones (§ 94).

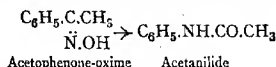
*Acetophenone*,  $C_6H_5.CO.CH_3$ , is a fragrant, crystalline substance, which melts at  $20^\circ$  and boils at  $202^\circ$ ; as a ketone it forms the usual crystalline condensation products.

Acetophenone is reduced by sodium amalgam to a crystalline secondary alcohol, *phenyl methyl carbinol*. When oxidised with chromic acid, it is converted into benzoic acid and carbon dioxide, but with alkaline permanganate the intermediate *benzoylformic* or *phenylglyoxylic acid* is also obtained ( $K=6.11$ ), the action being parallel to the conversion of acetic acid into oxalic acid by this agent (§ 122).



Many similar ketones have been prepared, having either two aryl radicals, or one aryl and one alkyl radical; like the higher alkyl ketones they do not form bisulphite compounds.

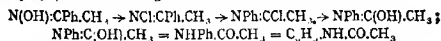
The oximes of these ketones are convertible into the isomeric anilides by a curious molecular transformation, in which the nitrogen atom enters the ketonic chain (Beckmann, 1887).



*Acetophenone-oxime*,  $C_6H_5.C(N.OH).CH_3$ , a crystalline substance melting at  $60^\circ$ , is formed by boiling an alcoholic solution of the ketone for two or three hours with the calculated quantities of hydroxylamine hydrochloride and caustic soda, which have previously been dissolved separately in the minimum amount of water; the product, which should be acidified if necessary, is poured into water, and the oxime is extracted with ether and recrystallised from alcohol or light petroleum.

The conversion into acetanilide is effected by gradually adding phosphorus pentachloride to the powdered oxime suspended in dry, alcohol-free ether; the ether is distilled off, the phosphorus compound removed by shaking with water, and the anilide recrystallised. *Benzophenone-oxime*,  $CPh_2.N.OH$ , which melts at  $140^\circ$ , is similarly converted into benzanilide.

The transformation of oximes into anilides and analogous compounds may be due to a molecular rearrangement of the *nitrogen chloride* which is formed transiently by the action of the phosphorus pentachloride on the oxime (compare Phenyl acetyl nitrogen chloride, § 252); the same transformation is effected by strong acids, especially in acetic acid solution. The oximes of unsymmetrical ketones, like the aldioximes, occur in stereoisomeric pairs,\* a labile synoxime, and a stable antioxime; it is the synoximes (§ 356) which undergo the Beckmann transformation.



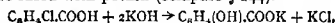
**273. Substitution Products of Benzoic Acid.**—Whilst benzoic acid is closely parallel to acetic acid in its action as an acid, as a benzene derivative it resembles the aromatic hydrocarbon; it readily forms substitution products with nitric and sulphuric acids, and the halogens.

As will be seen later, there are three classes of di-substitution products of benzene, the ortho-, meta-, and para-compounds, and the direct mono-substitution products of benzoic acid belong mainly to the second class; all the benzene hydrogen atoms can be substituted, however.

Meta-chloro- and meta-bromo-benzoic acids are readily formed by direct action of the halogen, whilst the ortho- and para-compounds are prepared indirectly, either from the aminobenzoic acids (see below) by the diazonium reaction, or by oxidising the corresponding bromotoluenes (§ 313).

The halogen benzoic acids are colourless crystalline substances of high melting point; owing to the influence of the halogen, they are stronger acids than the parent acid. *m-Chlorobenzoic acid*,  $C_6H_4Cl.COOH$  (*m*), melts at  $153^\circ$ ,  $K=0.0155$ ; the *o-acid* at  $137^\circ$ ,  $K=0.132$ ; *m-bromobenzoic acid*,  $C_6H_4Br.COOH$  (*m*), melts at  $155^\circ$ ,  $K=0.0137$ ; *pentachlorobenzoic acid*,  $C_6Cl_5.COOH$ , at  $200^\circ$ .

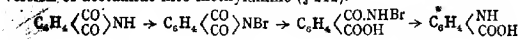
Owing to the presence of the electronegative carboxyl group, the halogen of these acids is also more easily displaced than that of the substituted benzenes; hydroxybenzoic acids (§ 308) are formed when the chloro-compounds are fused with potash (compare § 244).



The product obtained by nitrating benzoic acid with nitre and sulphuric acid consists mainly of *metanitrobenzoic acid* ( $K=0.0345$ ), but a certain amount of the ortho-isomeride is also formed; the two acids are separated by means of their barium salts, the ortho-salt being much the more soluble. Orthonitrobenzoic acid is more readily obtained by oxidising orthonitrotoluene (§ 316).

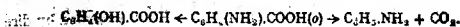
*o-Nitrobenzoic acid*,  $C_6H_4 \begin{smallmatrix} NO_2 \\ \diagup \\ COOH \end{smallmatrix}$  (*o*) is a sweet, but acid, crystalline substance, melting at  $147^\circ$ ;  $K=0.616$ . As a nitro-compound, it is reduced by tin and hydrochloric acid to the corresponding amine, orthoaminobenzoic acid.

This, however, is more economically manufactured from phthalimide (§ 324); it is formed from this substance by the action of hypobromites or hypochlorites (bleaching powder), the action being analogous to the conversion of acetamide into methylamine (§ 212).



*Anthranilic* or *o-aminobenzoic acid*,  $C_6H_4 \begin{smallmatrix} NH_2 \\ \diagup \\ COOH \end{smallmatrix}$  (*o*) (Fritzsche, 1841), is a crystalline substance, which melts at  $145^\circ$  and can be sublimed unchanged. It is akin to glycine in its actions—forms unstable salts with both acids and bases ( $K=0.0006$ ), is neutral to litmus, and is resolved by heat into aniline and carbon dioxide.

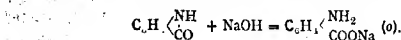
Anthranilic acid differs from the aliphatic compound in that it is convertible not only into the corresponding hydroxy-acid, salicylic acid (§ 308), but also by the diazonium interaction into chlorobenzoic acid, etc., and into benzoic acid itself.



*Methyl anthranilate*,  $NH_2.C_6H_4.COOMe$ , is a crystallisable oil, which is present in small quantity in orange and jasmine blossom, and when much diluted with alcohol resembles these flowers in odour.

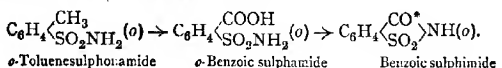
Anthranilic acid is of interest from its genetic connection with indigo (§ 337), from which it was first prepared by distillation with potash, and into which it is now reconverted synthetically on a manufacturing scale.

By reducing *o*-nitrobenzaldehyde (§ 277) with tin and hydrochloric acid, anthranil, an internal anhydride or lactame of anthranilic acid, is formed. Anthranil,  $C_6H_4 \begin{smallmatrix} NH \\ CO \end{smallmatrix}$ , is a liquid which boils and decomposes at about  $270^\circ$ , and has a characteristic odour: it cannot be made by dehydrating the acid, but is converted into it by boiling with alkalis.



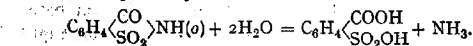
Benzoic acid is not sulphonated by ordinary sulphuric acid, but substitution can be effected by passing sulphuric anhydride vapour into the melted acid; *metasulphobenzoic acid*,  $C_6H_4 \begin{smallmatrix} SO_3H \\ COOH \end{smallmatrix} (m)$ , thus formed is a deliquescent, crystalline substance. The *ortho*- and *para*-acids are made indirectly, by oxidising the toluene-sulphonic acids (§ 314).

The imide of orthosulphobenzoic acid, the well-known sweet substance, saccharin, is made by oxidising orthotoluene-sulphonamide with potassium permanganate.



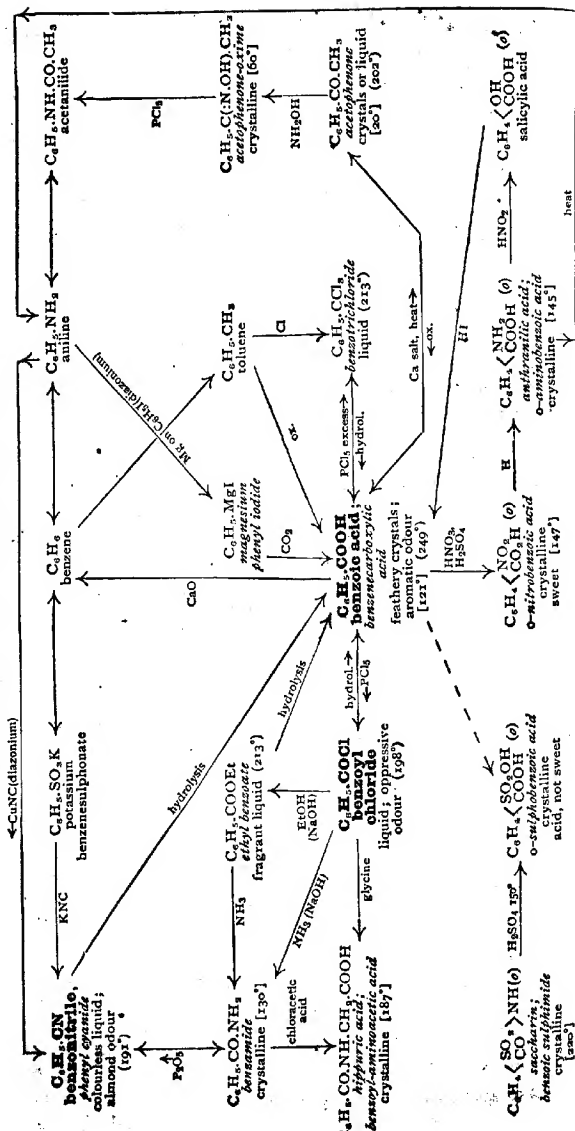
*Saccharin* or *benzoic sulphimide*,  $C_6H_4 \begin{smallmatrix} CO \\ SO_2 \end{smallmatrix} NH(o)$  (Remsen, 1879), is a crystalline substance, melting at  $220^\circ$ ; although very sparingly soluble in water, its solution is intensely sweet, 500 times sweeter than the corresponding solution of cane-sugar. The *sodium salt*,  $C_6H_4 \begin{smallmatrix} CO \\ SO_2 \end{smallmatrix} NNa$ , which it forms as an acid imide (§ 150), is freely soluble, and little less sweet.

When heated with concentrated sulphuric acid at  $150^\circ$ , saccharin is hydrolysed to orthosulphobenzoic acid, a substance having a very acid taste.



**274. Synopsis.**—Benzoic acid, a typical aromatic acid, bears the same relation to benzene as acetic acid to methane. It resembles the aliphatic compound in most of its actions, but as a benzene derivative readily forms substitution products.



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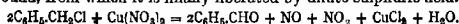
## CHAPTER XLIX

### BENZALDEHYDE : THE BENZAL RADICAL

**275. Benzaldehyde and the Benzal Radical.**—The aldehyde of benzoic acid is the well-known flavouring liquid, oil of bitter almonds. When almonds are subjected to pressure, a quantity of almond oil or glycerol trioleate (§133) is expressed, but on distilling the residue with steam, benzaldehyde and hydrocyanic acid pass over. These products result from the hydrolysis of the glucoside amygdalin (§ 171) by the accompanying enzyme emulsin.

Benzaldehyde is manufactured for the colour industry, etc., either by hydrolysing benzal chloride (below) by heating it with water and calcium carbonate, or by hydrolytically oxidising benzyl chloride (§ 280).

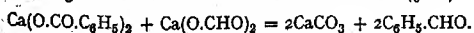
The latter process may be used in the laboratory; benzyl chloride or bromide is boiled in a reflux apparatus with water and copper nitrate, carbon dioxide being steadily passed through the vessel to remove the liberated oxides of nitrogen, which would otherwise oxidise the aldehyde to benzoic acid. When the benzyl chloride has disappeared, the aldehyde is extracted with ether, and purified by means of its crystalline bisulphite compound, from which it is finally liberated by dilute sulphuric acid.



*Benzaldehyde*,  $\text{C}_6\text{H}_5\text{CHO}$  (Liebig and Wöhler, 1832), is a colourless, highly refractive liquid, which boils at  $179^\circ$ , freezes at  $-13^\circ$ , and has the characteristic odour of essence of almonds.

The aromatic aldehyde resembles its fatty analogues in most respects. It is oxidised to benzoic acid by boiling with dilute nitric acid, or even by exposure to air (crystals of the acid are slowly formed when it is kept in an imperfectly stoppered bottle); and it reduces ammoniacal silver nitrate.

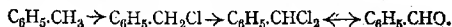
Conversely, benzoic acid is easily reduced to benzaldehyde by distilling its calcium salt with calcium formate (§ 82).



Like acetaldehyde, benzaldehyde is readily reduced to the

corresponding primary alcohol; and it colours bleached rosaniline. Similarly with phosphorus pentachloride, or better, carbonyl chloride, it yields a dichloride, *benzal* or *benzylidene chloride*,  $C_6H_5.CHCl_2$ , a liquid which boils at  $213^\circ$ , and like ethylidene chloride, is also formed by directly chlorinating the boiling monochloride (§ 280).

The radical  $C_6H_5.CH\cdot$  is known as the *benzylidene* or *benzal* radical, so that benzaldehyde may also be regarded as *benzoyl hydride* or *benzal oxide*.



**278. Additive Compounds and Condensation Products of Benzaldehyde.**—The additive compounds of benzaldehyde with sodium bisulphite and hydrocyanic acid are similar to those of acetaldehyde, but the bisulphite compound is much more readily formed. The ammonia compound is different, as the aldehyde condenses with the ammonia and does not combine additively with it (compare, however, Formaldehyde, § 86).

The various condensation products of benzaldehyde are similar to those of the aliphatic aldehydes, although more easily formed and better defined. The oxime, like most aldoximes and unsymmetrical ketoximes, exists in two stereoisomeric forms (§ 356), which differ in stability.

*Hydrobenzamide*,  $C_6H_5.CH(N:CH.C_6H_5)_2$ , which is formed as a white precipitate when benzaldehyde is shaken with aqueous ammonia, is a crystalline substance melting at  $110^\circ$ .

*Benzaldehyde phenylhydrazone*,  $C_6H_5.CH:N.NH.C_6H_5$ , is a crystalline substance, which melts at  $152^\circ$ , and reddens when kept. A similar crystalline condensation product, *benzylideneaniline*,  $C_6H_5.CH:N.C_6H_5$ , is formed by heating the aldehyde with aniline for an hour at  $100^\circ$ ; it can be recrystallised from water. *Benzaldehyde-semicarbazone*,  $C_6H_5.CH:N.NH.CO.NH_2$  (§ 227) melts at  $214^\circ$ .

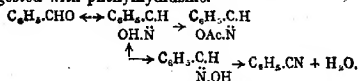
The labile modification of benzaldoxime is that which is obtained directly. Hydroxylamine hydrochloride is added slowly to an emulsion of benzaldehyde in strong caustic soda; after the action has finished, a little water is added, any unchanged benzaldehyde is extracted with ether, and the oxime is precipitated with carbon dioxide.

*Synbenzaldoxime*,  $C_6H_5.CH \begin{smallmatrix} \nearrow N.OH \\ \searrow N.OH \end{smallmatrix}$ , is a crystalline solid which melts at  $130^\circ$ ; when boiled it is gradually reconverted into the stable anti-form.

*Antibenzaldoxime*,  $C_6H_5.CH \begin{smallmatrix} \nearrow N.OH \\ \searrow OH.N \end{smallmatrix}$ , is a crystallisable oil which boils at  $124^\circ/14$  mm.; in contact with acids it is converted into the labile isomeride.

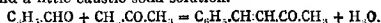
On boiling the stable antibenzaldoxime with acetic anhydride and sodium acetate, it is converted into an *acetate*,  $C_6H_5.CH:N.OAc$ , but under similar conditions the labile syn-oxime is dehydrated to benzonitrile.

The benzaldoximes are converted into benzaldehyde phenylhydrazone when digested with phenylhydrazine.



Unlike acetaldehyde, benzaldehyde does not condense with itself, although it polymerises under certain conditions (see Benzoin, § 355); but it condenses in the aldol-crotonaldehyde manner with many substances, the molecules of which contain the methyl or methylene group; with acetic acid it forms cinnamic acid (§ 332), the aromatic analogue of crotonic acid; and with acetone it yields benzylidene-acetone.

*Benzylidene-acetone*,  $\text{C}_6\text{H}_5\text{CH}:\text{CH}.\text{CO}.\text{CH}_3$ , a crystalline substance melting at  $42^\circ$ , is precipitated by simply warming the aldehyde with acetone and a little caustic soda solution.



The action of caustic soda on benzaldehyde is similar to its action on formaldehyde (§ 86), half the aldehyde being reduced to the corresponding alcohol (§ 280), and half oxidised to the acid.



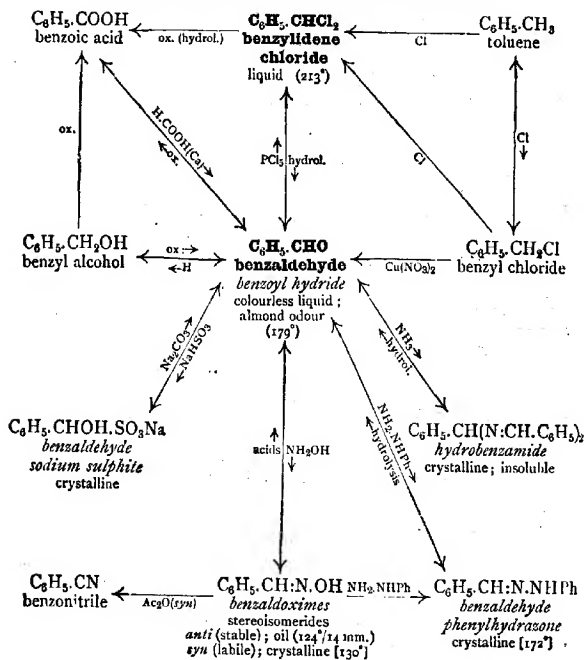
**277. Substitution Products of Benzaldehyde.**—Many substitution products of benzaldehyde have been prepared, although rarely by direct methods, as the aldehyde radical itself is attacked by substituting-agents (compare § 115). Benzaldehyde is thus converted into benzoyl chloride by direct chlorination, and the *chlorobenzaldehydes*,  $\text{C}_6\text{H}_4\text{Cl}.\text{CHO}$ , which are crystallisable liquids of high boiling-point (the *p*-compound melts at  $47^\circ$ ), are made indirectly, by hydrolysing chlorinated benzal chloride (§ 275), or oxidising chlorinated benzal-acetic (cinnamic) acid (§ 333).

*Orthonitrobenzaldehyde*,  $\text{C}_6\text{H}_4(\text{NO}_2).\text{CHO}$  (o), a crystalline substance melting at  $46^\circ$ , is made similarly by oxidising orthonitrocinnamic acid (§ 333) with permanganate (the *meta*-compound alone being formed by direct nitration); it combines with acetaldehyde, forming an additive compound from which indigo (§ 337) is precipitated by caustic soda.

*Orthoaminobenzaldehyde*,  $\text{C}_6\text{H}_4(\text{NH}_2).\text{CHO}$  (o), a crystalline substance melting at  $39^\circ$ , is formed by reducing the nitro-compound with ferrous sulphate and ammonia; it condenses with acetaldehyde, in presence of dilute caustic soda, to the aminoid compound quinoline (§ 386), the nuclear constituent of many of the vegetable alkaloids.

**278. Synopsis.**—Benzaldehyde, the aldehyde of benzoic acid, is a typical aromatic aldehyde. It resembles the higher fatty aldehydes in most respects, but forms condensation products more readily, and as a benzene derivative yields benzenoid substitution products.

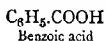
## BENZALDEHYDE: THE BENZAL RADICAL.



## CHAPTER L

### TOLUENE : THE BENZYL RADICAL

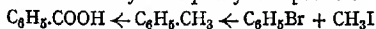
**279. Toluene.**—As benzoic acid is related to benzene in the same way as acetic acid to methane, it bears to the homologous hydrocarbon, methyl-benzene or toluene, a relation parallel to that which acetic acid bears to ethane.



The chief source of toluene is the unfrozen mother-liquor which is drained from the crystals of benzene during its purification (§ 243) ; it constitutes about 30 per cent. of crude commercial benzene.

The crude toluene is purified by fractional distillation, but can only be separated from paraffins of neighbouring boiling point by means of its sulphonic acid (§§ 314, 247). Toluene was first obtained in quantity by distilling balsam of Tolu, and can also be formed from the toluic acids (§ 321), and from benzene.

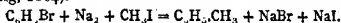
*Toluene* or *methylbenzene*,  $\text{C}_6\text{H}_5\cdot\text{CH}_3$  (Pelletier, 1832), is a light, mobile, insoluble liquid, which boils at  $110^\circ$  and freezes at  $-94^\circ$ , but otherwise resembles benzene. Its relation to benzene is proved by its slow oxidation to benzoic acid by hot, dilute nitric acid, and to benzaldehyde by chromyl chloride and water; the consequent presence of a methyl, as well as a phenyl radical in its molecule is confirmed by its synthesis from methyl and phenyl compounds.



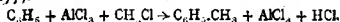
In the first synthesis, an equimolecular solution of bromobenzene and methyl iodide in dry ether is boiled in a reflux apparatus with the calculated amount of sodium; the addition of a few drops of ethyl acetate much accelerates the action.

As soon as the sodium is converted into sodium bromide and iodide, the cooled product is poured off and fractionated; some ethane first escapes, formed from the methyl iodide, and then the ether passes over,

accompanied by a little benzene, produced by the reduction of the bromo-derivative; finally, the crude toluene distils at about  $110^{\circ}$ , leaving a small residue of diphenyl (§ 353) in the flask. The toluene is then refractionated (Fittig, 1864).



The second method consists in passing methyl chloride vapour into a boiling solution of anhydrous aluminium chloride in benzene, when hydrogen chloride is evolved in abundance, and toluene and other methyl derivatives of benzene are formed. The aluminium chloride, as in all such condensations, remains unchanged and acts as a carrier, forming an unstable intermediate compound with the benzene and methyl chloride (Friedel and Crafts, 1877).



When hydrogen chloride ceases to be evolved, and the weight of the product has increased by an amount corresponding with the conversion of the benzene into toluene, the product is poured into water, and the light layer of hydrocarbon dried, and fractionated to separate unchanged benzene and higher homologues (§ 322, etc.).

These syntheses are of wide applicability; bromobenzene, for example, is thus convertible into ethylbenzene and propylbenzene.

**280. The Benzyl Radical: Toluene as Phenyl-methane.**—As toluene is both phenyl-methane and methylbenzene, it shows the characteristic properties both of a benzenoid and a paraffinoid hydrocarbon. It is readily nitrated and sulphonated, and when digested with chlorine in the cold and in presence of a carrier (preferably in the dark), forms substitution products (§ 313) which are homologous with and analogous in every respect to those of benzene.

But on passing chlorine into the boiling hydrocarbon in daylight (and not in presence of a carrier), the action is the same as with ethane. The hydrogen atoms of the methyl group are successively replaced by the halogen; benzyl chloride and benzal chloride are first formed, and finally benzotrichloride, identical with that which is obtained from benzoyl chloride by the action of phosphorus pentachloride.

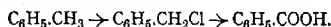


Benzyl and benzal chlorides correspond very closely with ethyl and ethylidene chlorides. The benzyl compound is readily prepared by passing chlorine into boiling toluene in a reflux apparatus until the necessary increase in weight is observed. The action proceeds only in daylight, and a carrier must not be used, or substitution is effected in the benzene nucleus; the product is simply fractionated to separate unchanged toluene and benzal chloride.

**Benzyl chloride**,  $\text{C}_6\text{H}_5\text{CH}_2\text{Cl}$  (Cannizzaro, 1853), is a colourless, insoluble liquid, which boils at  $179^{\circ}$ , and is aromatic and

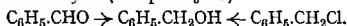
pleasant in odour, although very irritating to the eyes; the irritating action of the bromobenzene made from commercial benzene in daylight is due to the presence of benzyl bromide.

Benzyl chloride is reconverted into toluene by reduction with aluminium amalgam, and is easily oxidised to benzoic acid by boiling with dilute nitric acid; the chlorine is therefore in the methyl group or side chain, as it is termed, and not in the benzene nucleus.



Benzyl chloride is therefore the phenyl substitution product of methyl chloride; it behaves throughout as an aliphatic chloride. Whilst chlorobenzene is unaffected by alkalis, benzyl chloride is hydrolysed by boiling with sodium carbonate solution, or even with water—more easily than the aliphatic chlorides themselves.

The benzyl alcohol thus formed occurs naturally in various aromatic balsams and resins—as *benzyl benzoate* in balsam of Peru, but it is most readily obtained by the action of caustic soda on benzaldehyde (compare § 86).



On shaking this aldehyde with concentrated caustic soda solution (§ 276) heat is developed, and ultimately a permanent emulsion is formed with the liberated alcohol and benzoate; after a day or so, water is added to dissolve the benzoate, and the alcohol is extracted with ether and fractionated; it is unnecessary to dry the ethereal solution.

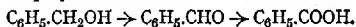
*Benzyl alcohol*,  $\text{C}_6\text{H}_5\cdot\text{CH}_2\text{OH}$  (Cannizzaro, 1853), is a colourless, sparingly soluble liquid, which boils at  $206^\circ$ , and has only a faint aromatic odour; it resembles the aliphatic alcohols in properties, and is a typical example of an aromatic alcohol.

It is reconverted into the chloride by phosphorus pentachloride, or even by heating with concentrated hydrochloric acid, and on warming with acetyl chloride it yields in the normal manner *benzyl acetate*, a fragrant liquid which is the chief constituent of oil of jasmine; when boiled with boric anhydride it is dehydrated to the corresponding ether, *benzyl ether*, an insoluble aromatic liquid, boiling at  $296^\circ$ ; and a similar mixed ether, *benzyl ethyl ether*, is formed by heating benzyl chloride with sodium ethoxide.

Benzyl alcohol is converted successively by mild oxidising agents, such as dilute nitric acid, into benzaldehyde and benzoic acid, i.e. an aldehyde and acid containing the same number of carbon atoms. It is thus a primary alcohol, the phenyl substitution-product of methyl alcohol.



The benzyl radical,  $C_6H_5\cdot CH_2$ , resembles the paraffinoid radicals, and enters into combination with other radicals in precisely the same way as ethyl; for this reason it is termed an aliphyl\* radical.

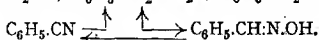


**281. Benzylamine and Phenylnitromethane.**—The primary amine, benzylamine, corresponding with benzyl chloride and benzyl alcohol, is closely akin to the aliphatic amines, and can be formed in all the ways in which the primary amines are made (§ 212).

It is produced, together with di- and tribenzylamine, when benzyl chloride is heated with alcoholic ammonia; it can be prepared by hydrolysing benzyl isocyanate with strong caustic soda solution, or by the action of alkalis on the bromamide of phenylacetic acid (§ 282); it is also formed by reducing benzonitrile with sodium in alcohol, or benzaldoxime with sodium amalgam in acid solution.

**Benzylamine**,  $C_6H_5\cdot CH_2\cdot NH_2$  (Mendius, 1862), is a soluble alkaline liquid, boiling at  $183^\circ$ . It is much more basic than aniline, and not only forms the ordinary crystalline, additive salts with strong acids, but even absorbs carbon dioxide.

Like the aliphatic primary amines, benzylamine is directly converted into its alcohol by nitrous acid, without the intermediate formation of a diazonium compound.



The corresponding nitro-compound, phenyl-nitromethane, is made by heating toluene with dilute nitric acid for many hours at  $100^\circ$ , or by the interaction of benzyl chloride and silver nitrite. It is isolated by conversion into its crystalline sodium derivative, from which it is then liberated by some comparatively feeble acid such as acetic acid; after extraction with ether, and distillation with steam, it is fractionated under reduced pressure.



**Phenyl-nitromethane** or *o*-nitrotoluene,  $C_6H_5\cdot CH_2\cdot NO_2$  (Gabriel, 1885), is a colourless, unstable liquid, which boils at  $160^\circ/35$ mm.; it resembles nitrobenzene in odour, and is similarly reduced by tin and hydrochloric acid to the corresponding amine, benzylamine.

In most respects, however, the toluene derivative resembles nitromethane, and is hydrolysed by hydrochloric acid at  $150^\circ$  to benzoic acid and hydroxylamine. Although a neutral substance, it slowly neutralises alkalis, and interacts with sodium methoxide, forming a crystalline sodium compound; it is therefore a pseudo-acid (§§ 259, 294).

**Sodium phenyl-isonitromethane**,  $C_6H_5\cdot CH\cdot NO\cdot ONa$ , is a deep yellow,

\* i.e. alkyl-phenyl.



When a concentrated solution of potassium cyanide is added to a paste of benzaldehyde sodium bisulphite, there is a vigorous action, the mass becomes liquid, and benzaldehyde hydrocyanide rises to the surface.

*Benzaldehyde-cyanhydrin* or *mandelonitrile*,  $C_6H_5.CHOH.CN$ , is an unstable oily liquid, which gives off hydrogen cyanide when heated alone, but when heated with concentrated hydrochloric acid in a reflux apparatus is rapidly hydrolysed to inactive mandelic acid.

*Mandelic acid*,  $C_6H_5.CHOH.COOH$  (Winckler, 1834), is a crystalline substance, melting at  $118^\circ$ ;  $K=0.0756$ . Although its molecule contains an asymmetrical nucleal atom, being a synthetic compound (§ 141) it is optically inactive; it is resolvable into optically active isomerides, however, by the usual methods, such as the fractional crystallisation of its cinchonine salt.

*d-Mandelic* and *l-mandelic acids* are crystalline substances melting at  $133^\circ$ ,  $[\alpha]_D = 156^\circ$ ; when melted together, they recombine, forming the inactive acid, m.p.  $118^\circ$ .

A partial separation is similarly effected by heating the "racemic" acid with laevo-menthol (§ 349) for an hour at  $155^\circ$ ; the *d*-mandelic acid is esterified, but the *l*-acid is practically unaffected, and can be removed by shaking the product with dilute alkali.

The relation of mandelic to phenylacetic acid is confirmed by its reduction to the latter when heated with hydriodic acid. The laevo-acid is also formed by direct hydrolysis of amygdalin with concentrated hydrochloric acid, so that the glucoside is represented by the formula,  $C_6H_5.CH(CN).O.C_{12}H_{21}O_{11}$ ; the active mandelic acids are rapidly racemised (§ 161) when heated.

**283. Synopsis.**—Toluene or phenyl-methane not only forms a series of products similar to those derived from benzene, but also a series in which the benzyl or phenylmethyl radical plays the part of an alkyl radical.



## CHAPTER LI

### CONSTITUTION OF BENZENE

**284. The Ring Formula.**—A sufficient number of aromatic or benzenoid compounds have now been considered to show that whilst in some respects they are similar to the compounds of the aliphatic group, they differ from them in many points. Although the molecule of the simplest benzenoid compound contains at least six carbon atoms, the relative proportion of elements other than carbon is smaller than in the preceding groups, and the aromatic compounds are richer in this element and poorer in hydrogen than their aliphatic analogues.

The benzenoid compounds rapidly interact with sulphuric and nitric acids, forming sulphonic and nitro-derivatives by substitution, whereas the paraffins practically cannot be sulphonated, and yield nitro-derivatives only with difficulty. The halogen substitution-products are also much more readily formed than those of the paraffins, and conversely are much more stable; unlike the halogen paraffins they are not directly oxidisable.

Again, although homology exists, as in the aliphatic group, the higher compounds are distinguished from compounds such as sugar by the stability of the six-carbon nucleus; in the oxidation of aromatic compounds there is practically no resting-place between this nucleus and carbon dioxide.

<sup>1</sup> Nevertheless, the homology of the higher aromatic compounds is the same as in the aliphatic group, and, as will be seen later, there are various series of compounds which are homologous with, and analogous in every respect to, phenol, aniline, benzoic acid, etc.

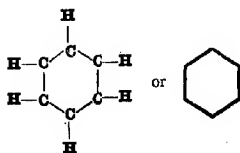
Benzene itself might be thought, from its molecular formula, to be an unsaturated hydrocarbon of the diacetylene or triolefine series, but it does not reduce cold alkaline permanganate like the olefines, and it combines additively with halogens with reluctance, the compounds thus formed being unstable, and readily reverting to the original condition.

When under certain circumstances additive compounds are formed, the number of univalent atoms added always falls short of the eight, which would be required in order to convert the benzene derivative into a derivative of the saturated hydrocarbon, hexane. Benzene itself combines only with six atoms of hydrogen or halogen, and benzoic acid takes up six atoms of hydrogen (§ 289), and no more.

Benzene therefore cannot be an olefine or acetylene, and apart from the fact that acetylene hydrocarbons of the same formula are known (§ 285), and have quite different properties, it is evident that the carbon atoms in benzene and its derivatives must be arranged in some manner essentially different from the arrangements obtaining in the aliphatic group (Kekulé).

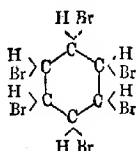
The assumption which best accounts for the properties of the aromatic compounds, is that in the six-carbon nucleus common to all of them, the carbon atoms are linked in a closed chain or ring, and that in the molecule of benzene, a hydrogen atom is linked to each carbon atom (Kekulé, 1865).

This ring formula is usually symbolised by a hexagon, a carbon atom being understood to be placed at each angle.



Hexagon or Ring Formula of Benzene

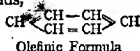
This formula accounts satisfactorily for the saturation of the benzene molecule by addition of only six halogen or hydrogen atoms; the two remaining atoms cannot be introduced without breaking the ring, and thus setting free the two carbon valencies employed in completing the ring linkage.



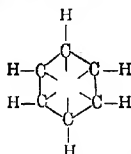
Benzene hexabromide

The only difficulty is in the disposal of the six free carbon valencies. It

was originally suggested that the carbon atoms are united by alternate paraffinic and olefinic bonds,



but this is inconsistent with the virtually saturated character of benzene and its indifference to cold alkaline permanganate. Various modifications have been proposed to obviate the difficulty. In the centric or isodynamic formula (Armstrong, 1887), which is now generally accepted, the surplus valencies are assumed to be directed towards the centre of the ring, each carbon atom exercising a general attraction over the others.



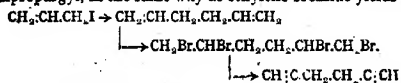
The Centric Formula of Benzene

This formula takes into account the great stability of the benzene nucleus (compare Fig. 24, § 326) and the reluctance with which it forms additive compounds. It is usual in practice, however, to use the plain hexagon.

The strongest confirmation of the ring formula for benzene is the thorough manner in which it accounts for the isomerism of the di- and higher substitution products (§ 298), but confirmation is also afforded by the nature of the reduction products, both of the hydrocarbon and of certain of its derivatives. Finally, the formula is completely justified by the synthesis of many benzenoid and reduced benzenoid compounds from open chain aliphatic compounds (§§ 287, 302, 305, etc.).

**285. Isomerides of Benzene.**—Two diacetylene derivatives isomeric with benzene have been prepared, and, as might be expected (Kekulé), their properties are entirely different from those of the aromatic hydrocarbon.

Dipropargyl, the first of these isomerides, can be made synthetically from allyl iodide. The iodide is boiled with sodium in ethereal solution, and thus converted into diallyl,  $\text{CH}_2\text{:CH}\cdot\text{CH}_2\text{:CH}_2\cdot\text{CH}\cdot\text{CH}_2$  (Berthelot, 1856) a liquid diolefine, which boils at  $59^\circ$ , and has a garlic odour. Diallyl, as a diolefine, combines with bromine, forming a tetrabromide, a crystalline substance, which melts at  $93^\circ$ , and resembles camphor in odour. Finally, when this tetrabromide is boiled with alcoholic potash, it loses all its bromine as hydrogen bromide, and is converted into the diacetylene hydrocarbon, dipropargyl, in the same way as ethylene bromide yields acetylene.



**Dipropargyl**,  $\text{CH}\text{:C}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{C}\text{:CH}$  (Henry, 1873). Is a

colourless liquid, boiling at  $86^{\circ}$ . It has all the properties of a highly unsaturated hydrocarbon, and an acetylene derivative; it combines readily with bromine and hydrobromic acid, forming respectively octobromo- and tetrabromo-hexane; it forms explosive derivatives with copper and other metals, and is very easily oxidised; permanganate converts it into carbon dioxide, and chromic acid mixture into carbon dioxide and oxalic acid.

This open-chain, highly unsaturated hydrocarbon thus has nothing in common with its isomeride benzene, except its molecular formula.

A second isomeride of the formula  $\text{CH}_3\text{C}:\text{C}:\text{C}:\text{CH}_3$ , is known, which differs from dipropargyl in that it does not form metallic compounds.

**286. Synopsis.**—To account for the special properties of the aromatic compounds, it is concluded that in the six-carbon nucleus common to them, the carbon atoms are arranged in a closed chain or ring, instead of in an open chain, as in the aliphatic compounds.



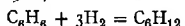
## CHAPTER LII

### THE CYCLOPARAFFINS AND THEIR DERIVATIVES

**287. The Naphthenes: Hexahydrobenzene.**—In addition to the paraffins, olefines and benzenoid hydrocarbons, natural petroleum contains naphthenes, hydrocarbons which are isomeric with the olefines, but are paraffinoid in character, and at the same time closely related to benzene.

The naphthenes are found in abundance in Caucasian and Galician petroleum (Beilstein, 1880); they are volatile liquids resembling the paraffins in odour, and when purified from benzenes and olefines are practically as inert; they are unaffected by fuming nitric and pyrosulphuric acids at the ordinary temperatures, and are only slowly attacked by bromine.

Similar hydrocarbons are obtained by reducing benzene and its homologues. When benzene is heated with excess of fuming hydriodic acid at  $280^{\circ}$ , it is reduced to a compound which has the composition of hexahydrobenzene (Wreden, 1877), and the properties of a naphthene (Beilstein, 1880). Hexahydrobenzene itself is readily prepared by passing dry hydrogen, saturated with benzene vapour, over reduced nickel at  $180$ – $200^{\circ}$  (Sabatier, 1901).



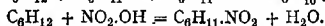
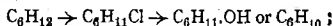
*Hexahydrobenzene* or *cyclohexane*,  $\text{CH}_2\langle\begin{smallmatrix} \text{CH}_2\cdot\text{CH}_2 \\ \text{CH}_2\cdot\text{CH}_2 \end{smallmatrix}\rangle\text{CH}_2$

(Baeyer, 1892), is a fragrant liquid, which boils at  $81^{\circ}$ , freezes at  $6^{\circ}$ , and has a specific gravity of 0.78 at  $15^{\circ}$ ; it was first prepared from quinitol (below).

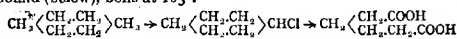
Although isomeric with the hexylenes, it has not the olefine character, but resembles the paraffins in its chemical behaviour. When treated with chlorine in diffused daylight at the ordinary temperature it forms substitutive, and not additive products, and these, like the haloid paraffins are either hydrolysed or dehalogenised by alkalis.

Concentrated sulphuric and nitric acids have practically no action on the hydrocarbon, in marked contrast to their rapid action on olefines and benzene; and it is slowly nitrated

by dilute nitric acid at  $120^{\circ}$ , in the same way as the higher paraffins (§ 231). Finally, it has no action on cold, dilute alkaline permanganate, whereas olefines instantly reduce this agent (§ 104).



*Chlorocyclohexane*,  $C_6H_{11}Cl$ , a liquid of peculiar, penetrating odour, boiling at  $143^{\circ}$ , resembles the chloroparaffins; when oxidised with nitric acid, it is converted quantitatively into adipic acid (§ 152). *Dichlorocyclohexane*,  $CHCl_2(CH_2)_4CHCl_2$ , boils at  $194^{\circ}$ . *Bromocyclohexane*,  $C_6H_{11}Br$ , which is most conveniently prepared from the corresponding hydroxy-compound (below), boils at  $163^{\circ}$ .

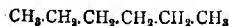


*Nitrocyclohexane*,  $C_6H_{11}.NO_2$ , a liquid boiling at  $206^{\circ}$ , resembles nitrobenzene in odour, but like the aliphatic nitroparaffins (§ 232) forms a crystalline sodium compound, and a red ferric compound. It is reduced by tin and hydrochloric acid to the corresponding amine, *aminocyclohexane*,  $C_6H_{11}.NH_2$ , a light, ammoniacal liquid boiling at  $134^{\circ}$ , which absorbs carbon dioxide and resembles the aliphatic amines.

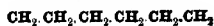
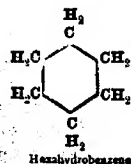
The entire behaviour of hexahydrobenzene shows that it is a saturated compound; the oxidation of its chloro-derivative to adipic acid indicates that it is a derivative of normal hexane; and its formation from benzene by a simple reduction points to the presence of a six-carbon ring in its molecule.

All these conditions are fulfilled by the above formula, in which the ring is formed by the linking of the terminal carbon atoms of the hexane chain, and each carbon atom remains fully saturated, as in the paraffins. Hexahydrobenzene is thus cyclohexane, a cycloid paraffin, a conclusion which is confirmed by various syntheses (below).

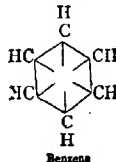
The formation of a carbon ring in the molecule makes little difference to the properties of the compound (§ 288).



Hexane

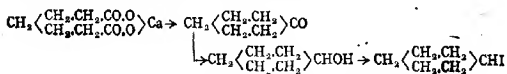


Cyclohexane



Similarly, hydroxycyclohexane (below) is entirely different from phenol in character; it has no acid properties, and closely resembles the corresponding open-chain secondary alcohols; like cyclohexane and the paraffins it is not affected by cold alkaline permanganate, and is therefore a saturated compound.

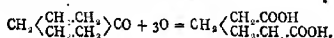
When *calcium pimelate*,\*  $\text{CH}_2(\text{CH}_2\text{CH}_2\text{CO}_2\text{O})_2\text{Ca}$  (§ 152), is heated, it is converted into a ketone, but as the two carboxyl groups co-exist in one molecule of the acid, the ketonic alkyl groups remain linked together. The resulting ketohexamethylene is reduced by sodium amalgam to the corresponding secondary alcohol, hydroxycyclohexane, and this is converted into its iodide by hydriodic acid; on reducing the iodide with a zinc-copper couple, it is converted into cyclohexane.



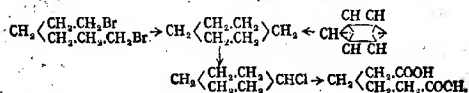
*Ketohexamethylene*,  $\text{CH}_2\langle\begin{smallmatrix}\text{CH}_2\text{CH}_2 \\ \text{CH}_2\text{CH}_2\end{smallmatrix}\rangle\text{CO}$  (Mayer, 1893) is a liquid of peppermint odour, boiling at  $155^\circ$ . *Hydroxycyclohexane* or *hexahydrophenol*,  $\text{CH}_2(\text{CH}_2\text{CH}_2)\text{CHOH}$  (Baeyer, 1893), is a crystallisable liquid of fusel odour, which boils at  $161^\circ$ ; it is also formed by reducing the corresponding *iodhydrin* (from quinitol, § 306, and hydriodic acid), and by hydrogenating phenol at  $220^\circ$  by the nickel method (above).

When heated with concentrated hydrobromic acid, hydroxycyclohexane is converted into the corresponding bromo-compound, whilst as a secondary alcohol it is reconverted into the ketone by gentle oxidation.

Ketohexamethylene closely resembles the aliphatic ketones; its carbon chain is broken in the normal manner on further oxidation, with production of adipic acid,—the only difference from an aliphatic ketone being that the two alkyl groups remain linked together.



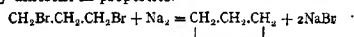
Another synthesis of hexamethylene is afforded by *ω'-dibromohexane*,  $\text{CH}_2\text{Br}(\text{CH}_2)_4\text{CH}_2\text{Br}$ , an unstable liquid of high boiling-point, which can be made synthetically from allyl bromide; it is converted into cyclohexane when heated with sodium (Perkin, jun., 1894; compare *Trimethylene*, § 288). Cyclohexane derivatives can also be made by a modification of the malonic acid synthesis (§ 289).



\* *Pimelic acid* is best made by the cyanide synthesis from *pentaerythrene dichloride*, which is formed, together with benzonitrile, by the action of phosphorus pentachloride on piperidine (§ 388).

**288. Trimethylene and the Cycloparaffins: the Tension Hypothesis.**—The saturated hydrocarbons of the type of cyclohexane form a most important connecting link between the aliphatic and aromatic series. The first member of this series is cyclopropane; it is made by debrominating *trimethylene bromide*, an isomeride of propylene bromide which is formed by the action of hydrobromic acid on allyl bromide (§ 215).

When trimethylene bromide is boiled with sodium, sodium bromide is formed, and a gas is steadily evolved, which is isomeric with propylene, although very different in properties.

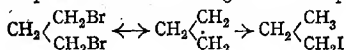


*Trimethylene* or *cyclopropane*,  $\text{CH}_2\langle\begin{smallmatrix} \text{CH}_2 \\ \text{CH}_2 \end{smallmatrix}\rangle$  (Freund, 1881), is

an easily condensible gas, which burns with a smoky flame like propylene, but differs from it in its action with halogens and halogen acids. It is absorbed by bromine, very slowly, regenerating trimethylene bromide; and although it combines fairly rapidly with fuming hydriodic acid, normal propyl iodide is formed, instead of the secondary iodide which is obtained by the action of this agent on propylene.

Trimethylene has no action on cold alkaline permanganate (§ 104), and when chlorinated is converted into a substitution-product, *dichlorocyclopropane*,  $\text{C}_3\text{H}_4\text{Cl}_2$ , which differs from the chlor-olefines in being unaffected by nitric acid.

It is obviously not an olefine, and the only alternative constitution is that which is represented by the ring or cycloid formula; this not only explains the saturated character of the hydrocarbon (all the carbon atoms being quadrivalent), but also accounts for the formation of terminally ( $\omega$ -) substituted products when the ring is broken open.



Trimethylene bromide      Trimethylene      *n*-Propyl iodide

The homologues of trimethylene are present in petroleum, and several of them have also been made synthetically; they behave almost entirely as saturated compounds.

*Cyclopentane*,  $\text{CH}_2(\text{CH}_2)_3\text{CH}_2$ , which is formed synthetically from calcium adipate, boils at  $51^\circ$ . *Methylcyclopentane*,  $\text{C}_6\text{H}_{10}\text{CH}_3$ , which boils at  $72^\circ$ , is formed by the action of hydriodic acid on benzene, probably owing to isomeric change of cyclohexane, with which it constitutes the *hexanaphthene* of petroleum. *Cyclohexane*,  $\text{CH}_2(\text{CH}_2)_4\text{CH}_2$ , boils at  $81^\circ$ ; its *methyl derivative*,  $\text{C}_7\text{H}_{12}$ , which boils at  $97^\circ$ , is *hexahydrotoluene*, and the principal constituent of *heptanaphthene*.

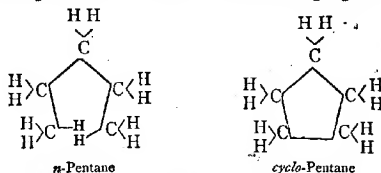
Corresponding unsaturated cycloid hydrocarbons such as the dihydrobenzenes and tetrahydrobenzene (§ 290) have also been prepared; these are highly reactive, unsaturated compounds, the existence of which forms very strong evidence for the centric constitution of benzene.

The varying stability of saturated cycloid compounds is explained by a stereometric hypothesis (Baeyer, 1885-1890), which also accounts for the progressive instability of olefinic and acetylenic compounds (§§ 105, 110), and throws light on the conditions determining the formation of lactones (§ 151) and dibasic anhydrides (§ 152).

We have seen that the isomerism of optically active compounds (§§ 140, 141), and compounds of the type of maleic and fumaric acids (§ 155) necessitates the assumption that the four valencies of the carbon atom are distributed symmetrically in space; they proceed radially through the four angles of a tetrahedron, from the centre, at which the atom is situated.

From this it follows that the atoms which constitute a carbon chain cannot lie in a straight line, but must form an open polygon, the angle of which is equal to the angle between these valency directions (compare § 326).

As this angle is approximately  $109.5^\circ$ , whilst that of a regular pentagon is  $108^\circ$ , it follows that the open chain of *n*-pentane forms, without strain, very nearly a closed pentagon, closely approximating to that of cyclopentane; hence the cycloid is practically as stable as the normal molecule, and the compounds are almost identical in properties.



Similar Configuration of Normal and Cyclopentane Compounds.

The valencies, however, represent centres of attraction, and it is therefore permissible to assume that their relative positions in space are not absolutely fixed, but are alterable under constraint (Baeyer). This simple assumption is justified by the consequences, for by its aid the apparent paradox of the lessened stability of double (and triple) linkages is removed; molecules containing such linkages are in a highly strained condition, which can only be relieved by their reversion to the free, singly-linked form.

The amount of resistance or "tension" set up by closing the above pentagon is almost negligible, the total angular displacement of each valency being  $0.75^\circ$ . Hence saturated rings of five atoms should be more stable than any others. Cyclopentane, in fact, is the most stable of the

cycloparaffins; it does not unite with bromine, and the six-carbon naphthenes are converted into its alkyl derivatives by heating with hydriodic acid. Similarly,  $\gamma$ -hydroxy-acids and  $\gamma$ -dicarboxylic acids form anhydrides more readily than any others.

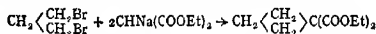
In an olefinic linkage, however, the valencies are parallel, and each valency or direction of attraction is therefore displaced through  $54.75^\circ$ ; the tension thus set up is very large, and the "ring" opens with great ease. Although the two olefinic carbon atoms are connected by double valencies, the strain set up by forcing these valencies into parallel positions is therefore such as to render the molecule highly unstable, and ready to revert to the free and stable singly-linked form. The special instability of olefines towards oxidising agents follows (§ 105) from a preliminary additive conversion into alcohols or glycols (thereby relieving the strain); but with other additive agents the resulting single linkage remains intact, and the molecule is not broken up.

Trimethylene and tetramethylene are more stable than ethylene, but less stable than cyclopentane, the angles of "tension" being respectively  $24.75^\circ$  and  $9.75^\circ$ \*; hence trimethylene readily forms additive compounds, although not so readily as ethylene, but does not interact with cold, alkaline permanganate. Hexamethylene is, however, less stable than cyclopentane, as the coil of atoms has now to be forced open to make the ring; the angle of "tension" is  $-5.25^\circ$ .\*

On the other hand, however, it appears that in the synthesis of cycloidal dicarboxylic acids (§ 289) from the corresponding monobrominated, open-chain, dicarboxylic esters, trimethylene derivatives are formed with much greater ease than those containing four, five and six-membered saturated carbon rings (Perkin, jun., 1905).

**289. Synthetic Cycloparaffinoid Compounds.**—The cycloparaffins form alcohols, acids, amides, etc., which closely resemble, and are in every respect analogous to the corresponding open-chain paraffin derivatives. Many of these compounds have been made synthetically by means of ethyl malonate, and in other ways (Perkin, jun., 1883, et seq.).

When trimethylene bromide is heated in alcoholic solution with ethyl sodiomalonate, a double substitution is effected, and ethyl trimethylene-malonate is formed, a second molecule of the sodiomalonate being converted into ethyl malonate; the substituted malonate is then converted into the free acid, as in the synthesis of alkylacetic acids (§ 148a). A better yield is obtained by substituting ethyl cyanacetate for the malonate (§ 148a), the mechanism of the process being very similar.



*Tetramethylene-dicarboxylic or trimethylene-malonic acid*,  $\text{CH}_2 \begin{pmatrix} \text{CH}_2 \\ \text{CH}_2 \end{pmatrix} \text{C}(\text{COOH})_2$ , melts at  $157^\circ$ ; the corresponding cyanacetic derivative,  $\text{C}_4\text{H}_6(\text{CN}).\text{COOH}$ , melts at  $70^\circ$ , and is readily hydrolysed to the malonic acid.

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\*  $\frac{109.5-60}{2}$ ;  $\frac{109.5-90}{2}$ ;  $\frac{109.5-120}{2}$

When heated above its melting-point, trimethylene-malonic acid is resolved in the characteristic malonic fashion into carbon dioxide and the corresponding monocarboxylic acid

*Tetramethylene-carboxylic acid*,  $\text{CH}_2\langle\begin{smallmatrix} \text{OH}_2 \\ \text{CH}_2 \end{smallmatrix}\rangle\text{CH.COOH}$  (Perkin, jun., 1884), is a liquid which boils at  $191^\circ$ , and resembles butyric acid in odour; it forms the usual acid derivatives.

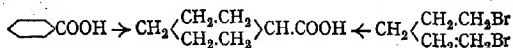
The *acid chloride*,  $\text{C}_4\text{H}_7\text{COCl}$ , boils at  $143^\circ$ , and the *acid anhydride*,  $(\text{C}_4\text{H}_7\text{CO})_2\text{O}$ , at  $160^\circ$ ; the *ethyl ester*, which is formed in the usual way, boils at  $160^\circ$ , and is convertible into the *amide*,  $\text{C}_4\text{H}_7\text{CONH}_2$ , a crystalline substance melting at  $138^\circ$ , which may also be formed by distilling the *ammonium salt*; the *nitrile*,  $\text{C}_4\text{H}_7\text{CN}$ , formed from the amide, is a liquid boiling at  $150^\circ$ , and is hydrolysed to the acid in the normal manner.

The amide is converted by hypobromite and alkali (§ 212) into *aminocyclobutane*,  $\text{C}_4\text{H}_7\text{NH}_2$ , a pungent alkaline oil boiling at  $51^\circ$ , which in turn is converted by nitrous acid into the alcohol, *hydroxycyclobutane*,  $\text{C}_4\text{H}_7\text{OH}$ ; this is a liquid boiling at  $123^\circ$ , which resembles butyl alcohol in odour, and is convertible into the corresponding *bromide*,  $\text{C}_4\text{H}_7\text{Br}$ , a heavy liquid boiling at  $104^\circ$ .

On distilling *calcium tetramethylene-carboxylate* with calcium formate it is reduced to the corresponding *aldehyde*,  $\text{C}_4\text{H}_7\text{CHO}$ , a liquid boiling at  $117^\circ$ , but the hydrocarbon cannot be made by distilling the sodium salt with lime, as a complex decomposition ensues. The corresponding *primary alcohol*,  $\text{C}_4\text{H}_7\text{CH}_2\text{OH}$ , is formed by reducing the acid chloride with sodium in moist ether, and the *amine*,  $\text{C}_4\text{H}_7\text{CH}_2\text{NH}_2$ , an alkaline, ammoniacal liquid boiling at  $83^\circ$ , is formed by reducing the nitrile; it forms the usual *platinichloride*, etc.

Other series of cycloparaffinoid compounds have been prepared in the same way. The trimethylene derivatives are made from ethylene bromide; *trimethylene-carboxylic acid*,  $\text{C}_3\text{H}_5\text{COOH}$ , is a liquid resembling propionic acid, and boiling at  $190^\circ$ ; its *ethyl ester* is a fragrant liquid boiling at  $93^\circ$ .

*Hexamethylene-carboxylic* or *hexahydrobenzoic acid*,  $\text{C}_6\text{H}_{11}\text{COOH}$ , a crystalline compound which melts at  $28^\circ$  and boils at  $232^\circ$ , resembles valeric acid in odour and acidity;  $K = 0.0013$ . It is formed similarly, although in small quantity, from pentamethylene dibromide,\* but is best prepared by reducing benzoic acid with sodium in amyl alcohol; its *ester* resembles ethyl valerate.



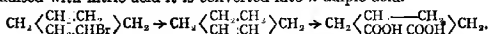
\* Pentamethylene dibromide is made from pentamethylene diamine (§ 215) through the corresponding glycol; see also *dichloride*, § 287.

*Hexahydrotoluic acid*,  $\text{CH}_3\text{C}_6\text{H}_{10}\text{COOH}$ , a crystalline solid melting at  $41^\circ$ , is made by reducing *o*-toluic acid (§ 321) in the same manner; a liquid stereoisomeride has been prepared synthetically. Analogous di- and tetra-carboxylic acids have also been synthesised, and as a rule exist in stereoisomeric pairs (compare Reduced Phthalic Acids, § 326).

**290. Cyclo-Olefines: Partially Reduced Benzenes.** — When chlorocyclohexane or bromocyclohexane is heated with the aminoid base, quinoline (§ 386), it loses an equivalent of hydrogen halide, and is converted into an unsaturated cycloid olefine, tetrahydrobenzene.

*Tetrahydrobenzene*,  $\text{CH}_2\langle\begin{smallmatrix}\text{CH}_2\cdot\text{CH}_2 \\ \text{CH}:\text{CH}\end{smallmatrix}\rangle\text{CH}_2$  (Baeyer, 1894), is a liquid which has a somewhat alliacious odour, and boils at  $82^\circ$ ; it is unstable, and like the turpentine hydrocarbons rapidly polymerises to a thick gum.

Tetrahydrobenzene is an ethylene derivative, as it decolorises cold dilute alkaline permanganate, and forms with bromine an additive dibromide; 1:2-dibromocyclohexane,  $\text{C}_6\text{H}_{10}\text{Br}_2$ , is an unstable oily liquid. The hydrocarbon further resembles certain terpenes (§ 350) in forming a crystalline *nitrosochloride*,  $\text{C}_6\text{H}_{10}\text{NOCl}$ , with nitrosyl chloride. When oxidised with nitric acid it is converted into *n*-adipic acid.



The dichlorocyclohexanes and dibromocyclohexanes similarly yield dihydrobenzenes when heated with quinoline (Baeyer, 1894); these, however, exist in two isomeric forms, differing in the position of the ethylene linkages.

$\Delta^1,4$ -Dihydrobenzene,\*  $\text{CH}_2\langle\begin{smallmatrix}\text{CH}\cdot\text{CH} \\ \text{CH}:\text{CH}\end{smallmatrix}\rangle\text{CH}_2$  (Fortey, 1898), made from 1:4-dichlorocyclohexane (§ 287), is a light unstable liquid, which boils at  $82^\circ$ , and resembles tetrahydrobenzene in odour; it combines with bromine forming a crystalline *tetrabromide*, melting at  $184^\circ$ , and is therefore a diolefinic compound.

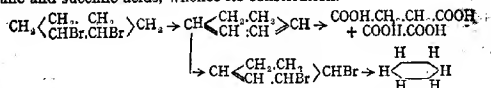
$\Delta^1,3$ -Dihydrobenzene,  $\text{CH}\langle\begin{smallmatrix}\text{CH}_2\cdot\text{CH}_2 \\ \text{CH}:\text{CH}\end{smallmatrix}\rangle\text{CH}$  (Crossley, 1904), which is prepared from tetrahydrobenzene dibromide (above), is a liquid of strongly alliacious odour, boiling at  $82^\circ$ ; like its isomeride it is unstable, and slowly polymerises to a jelly. It combines readily with bromine, forming a crystalline *dibromide*, melting at  $108^\circ$ , which when heated with quinoline loses all its bromine as hydrogen bromide, and is converted into benzene.

This dibromide can be further brominated, but with difficulty; the second dihydrobenzene is in fact probably not a diolefine as represented, but partially benzenoid in constitution.

\* For explanation of this nomenclature see Reduced Phthalic Acids, § 326.



$\Delta^{1,3}$ -Dihydrobenzene gives a very characteristic colour reaction with nitric acid, and when further oxidised with this agent is resolved into oxalic and succinic acids, whence its constitution.



Tetrahydrobenzene and the dihydrobenzenes form a complete series connecting cyclohexane with benzene, and well illustrate the transition from the open, paraffinoid, to the centric, benzenoid structure.

The boiling-points of these hydrocarbons lie very close together, but their specific gravities steadily increase as the percentage of hydrogen diminishes; and their other physical properties change in a similar way.  $\Delta^{1,3}$ -Dihydrobenzene is closely allied to benzene, whilst tetrahydrobenzene is a pure olefine, having the ordinary olefinic relation to the corresponding paraffinoid hydrocarbon, cyclohexane.

Hydrocarbon	B. p.	Sp. gr. at 15°
Cyclohexane . . . . .	81°	0.777
Tetrahydrobenzene . . . . .	84°	0.803
$\Delta^{1,3}$ -Dihydrobenzene . . . . .	82°	0.838
$\Delta^{1,4}$ -Dihydrobenzene . . . . .	82°	0.850
Benzene . . . . .	81°	0.879

The reduced benzenes are of further interest in that they are closely related to certain terpenes (§ 347). *Dihydrocymene*,  $\text{CH}_3 \cdot \text{C}_8\text{H}_8 \cdot \text{CHMe}_2$  (Baeyer, 1893), which is prepared synthetically in much the same way as the dihydrobenzenes, not only has the chemical character of the terpenes, but also the turpentine odour.

**291. Synopsis.**—The cycloparaffins and their substitution products are saturated ring-compounds, which are intimately related to the normal paraffins, and closely resemble them in behaviour; they are also genetically connected with the aromatic hydrocarbons, and can be made synthetically from open-chain compounds. Several of the corresponding cyclo-olefines are also known.



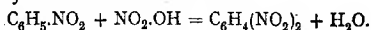
## SECTION XIII

### THE POLY-SUBSTITUTION PRODUCTS OF BENZENE

#### CHAPTER LIH

##### COMPLEX NITRO- AND AMINO-COMPOUNDS

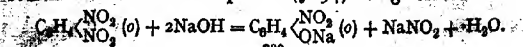
**292. The Poly-Nitrobenzenes.**—If in nitrating benzene, the hydrocarbon is poured into the acid mixture, so that it is always surrounded by excess of the latter, and the mass is heated instead of being kept cool, three isomeric dinitrobenzenes are formed; and the same compounds are produced in this way from nitrobenzene itself.



The heavy oily product is poured into water, and as soon as it has set to a crystalline mass is well washed, and repeatedly recrystallised from hot alcohol, in which the principal constituent, meta-dinitrobenzene, is less soluble than its isomerides. The ortho-compound is separated by evaporating the alcoholic mother liquor, and pouring the solution of the residue in boiling nitric acid into a large excess of the cold acid; finally, a small quantity of the para-compound may be precipitated from the acid mother liquor with water.

*Metadinitrobenzene*,  $\text{C}_6\text{H}_4(\text{NO}_2)_2(m)$  (Deville, 1841), crystallises in almost colourless needles, and melts at  $90^\circ$ ; it is usually yellowish from impurity. *Orthodinitrobenzene* melts at  $116^\circ$ , and the *para*-compound at  $172^\circ$ . All three compounds boil at about  $300^\circ$  without being decomposed.

The dinitrobenzenes are neutral substances, which resemble the mononitro-compound in chemical character; their hydrogen is not acidic, but one of the nitro-groups in the ortho-compound is detachable by hydrolysis with caustic soda, the sodium salt of orthonitrophenol (§ 294) being formed.

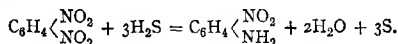


Similarly a nitro-group is replaced by ethoxyl, yielding the corresponding *nitrophenetole* (compare § 254), when either the ortho- or para-compound is heated with alcoholic sodium ethoxide; but the meta-compound is not affected by alkalis.

Although stable under ordinary conditions, the dinitrobenzenes can be exploded by detonation with mercuric fulminate; the mixture obtained by nitrating crude benzene is used in blasting, under the name of "roburite."

By further nitrating the dinitrobenzenes, a third nitro-group can with difficulty be introduced, but no more; the meta-compound yields *symmetrical trinitrobenzene*, melting at 121°, and the ortho- and para-compounds an isomeric product, melting at 57° (§ 299). A *tetranitrobenzene* has been prepared indirectly from trinitrophenol.

**293. The Nitranilines: Influence of Substituent Groups.**—By means of alcoholic ammonium sulphide, the agent originally used in the reduction of nitrobenzene, the dinitrobenzenes can be reduced to nitranilines; the second nitro-group remains intact as long as any of the original dinitro-compound is present, and metanitriline is conveniently prepared in this manner.



The alcoholic, ammoniacal solution of the dinitrobenzene is alternately saturated with sulphuretted hydrogen, and heated on a water bath in a reflux apparatus, until the requisite increase in weight, due to the sulphur and eliminated water, is obtained. The product is poured into hot water, and the nitraniline dissolved out from the washed precipitate with dilute hydrochloric acid, and reprecipitated with ammonia. It may be recrystallised either from hot water, or from alcoholic ammonia.

*Metanitriline*,  $\text{C}_6\text{H}_4(\text{NO}_2).\text{NH}_2(m)$ , (Muspratt and Hofmann, 1846), crystallises in yellow needles, melts at 114°, and boils at 286°. The corresponding ortho- and para-compounds may be made in a similar manner, but are more conveniently obtained by nitrating acetanilide.

Aniline itself is decomposed by concentrated nitric acid, and can only be nitrated in presence of sulphuric acid, and then principally the meta-compound is formed. If, however, an acetyl group be introduced into the amino-group, by means of acetyl chloride or acetic acid, the group is protected from the action of the substituting agent, and substitution can be effected in the benzene ring in the normal manner.

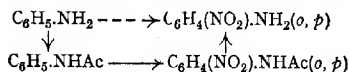
In this way, acetanilide can be converted into ortho- and para-nitroacetanilides, and from these the respective nitranilines.

lines can be readily obtained; the halogen-substituted anilines are also very conveniently prepared in this manner.

The acetanilide is slowly added to cold fuming nitric acid, the temperature not being allowed to rise, and the deep red solution is diluted by pouring on pounded ice. Water is then added, and the precipitated yellow nitro-compound, which consists principally of paranitracetanilide, is well washed and dried, and purified from the ortho-compound by washing with cold chloroform; the two compounds are finally recrystallised from hot alcohol.

*Paranitracetanilide*,  $C_6H_4(NO_2).NHAc$  (*p*), (Grethen, 1875), crystallises in colourless needles, and melts at  $207^\circ$ ; the *ortho*-compound forms orange plates, and melts at  $78^\circ$ . Like acetanilide, these compounds are readily hydrolysed; after boiling for a short time with concentrated hydrochloric acid, the nitraniline can be precipitated with caustic soda.

*Orthonitraniline* crystallises in orange needles, and melts at  $71^\circ$ ; the *para*-compound is colourless, and melts at  $147^\circ$ .

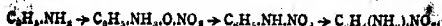


These compounds are much less basic than aniline, owing to the acidifying influence of the nitro-group; their salts are unstable, and the amino-groups of the ortho- and para-compounds are detachable by alkaline hydrolysis, yielding the corresponding nitrophenols. The nitranilines are thus less akin to the amines than aniline, and more akin to the amides.

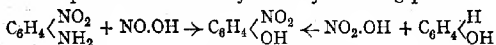
Metanitriline is the most basic of the three; the ortho-compound shows practically no tendency to form a hydrochloride in aqueous solution, although on the other hand it has no acidic properties (compare Nitrophenols, § 294). The acidifying influence of the nitro-group is considerably greater than that of the halogens; this group is in fact the most electro-negative of the ordinary substituent groups, which may be arranged in the following order as regards their influence on the dissociation constant of aniline: nitro-group, carboxyl, phenyl-diazonium-group, bromine, chlorine, methyl, methoxyl.

In the nitration of amino-compounds, as in their sulphonation and chlorination (§ 252), intermediate compounds are formed in which the group which eventually enters the benzene nucleus, temporarily replaces the amino-hydrogen; in the case of the amines, these compounds are identical with the nitramines or diazoic acids (§ 259).

Phenylnitramine, formed by the action of nitric anhydride on aniline, or by dehydrating aniline nitrate with acetic anhydride, is isomerised by mineral acids to a mixture of *o*- and *p*-nitranilines; and the substituted phenylnitromethanes undergo a similar change (Bamberger, 1895).



**294. The Nitro- and Amino-Phenols.**—The nitranilines are also converted into the nitrophenols by nitrous acid (§ 255), and metanitrophenol is conveniently prepared in this manner; it crystallises on concentrating the product. Ortho- and para-nitrophenol are made by directly nitrating phenol.



The phenol is simply digested with cold dilute nitric acid for a few hours, and the oily product, after well washing with cold water, is distilled with steam. The ortho-compound passes over with the steam, and collects with the water in bright yellow crystals, whilst the colourless para-compound is extracted from the tarry residue with boiling water.

*Orthonitrophenol*,  $\text{C}_6\text{H}_4(\text{NO}_2).\text{OH}$  (o) (Hofmann, 1857), is a golden yellow, crystalline substance, which melts at  $45^\circ$ . It differs very remarkably from its isomerides, as it has a characteristic odour, is sweetish in taste, and is volatile with steam. *Metanitrophenol* forms only pale yellow crystals, and melts at  $96^\circ$ , whilst *paranitrophenol* is colourless, and melts at  $114^\circ$ ; neither is volatile with steam, nor has any odour.

For the same reason that the nitranilines are less basic than aniline, the nitrophenols are more acidic than phenol,\* and all three compounds form stable metallic salts. *Sodium orthonitrophenol* is intensely crimson in colour, whilst the *para-compound* is golden yellow, and the *meta-compound* colourless.

The nitrophenols are converted by phosphorus pentachloride into nitrochlorobenzenes, analogous to acid chlorides. The ortho- and para-chlorides are readily hydrolysed by caustic soda, and are converted by ammonia into the corresponding nitranilines, from which, however, they may also be made by the diazonium interaction.

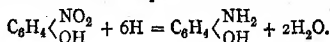
It is probable that *o*-nitrophenol is differently constituted from its isomerides, and is, in part at all events, a nitroic acid derivative (§ 232), having a quinonoid structure (§ 362),  $\text{O}:\text{C}_6\text{H}_3:\text{NO.OH}$ ; the coloured phenolic salts are probably derived from such labile acids, whilst nitro-compounds such as *m*-nitrophenol, which are colourless or nearly colourless, have the stable nitro-constitution.

The colourless modifications or true nitrophenols appear to be pseudo-acids, analogous to phenylnitrosamine (§ 259), formonitrile (§ 205), and the stable nitroparaffins (§§ 232, 281), whilst the coloured, quinonoid modifications contain the acid nitroic radical,  $:\text{NO.OH}$  (compare Picric acid, § 295). A hydrogen atom becomes acidic only when linked to a doubly or triply linked multivalent atom (§§ 232, 233), its instability or chemical activity being apparently connected with the strained condition of the molecule (§ 286).

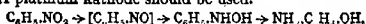


\*  $\text{K} = 0.000043$  (ortho),  $0.000012$  (para),  $0.000006$  (meta).

By reducing the nitrophenols, conveniently with aluminium amalgam and water, aminophenols are obtained.



*p*-Aminophenol is also formed quantitatively by the isomerising action of mineral acids on phenylhydroxylamine (§ 263), and is therefore readily prepared by electrolysis of a solution of nitrobenzene in concentrated sulphuric acid; the nitro-group is successively reduced to the nitroso- and hydroximino-groups, but the action cannot proceed further, as the hydroxylamine derivative is instantly isomerised, forming *p*-aminophenol sulphate. A platinum cathode should be used.



The aminophenols are unstable, easily oxidised substances, which soon turn brown in air; they can only be distilled, even with steam, if air be excluded by means of carbon dioxide or hydrogen sulphide. On account of their reducing action they are used as photographic developers.

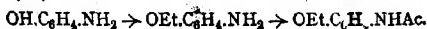
*Paraminophenol*,  $\text{NH}_2\text{C}_6\text{H}_4\text{OH}$  (*p*), a crystalline substance melting at  $184^\circ$ , is known technically as "paramido phenol"; the sulphate of its methyl derivative, *p*-methylaminophenol,  $\text{NHMe.C}_6\text{H}_4\text{OH}$  (*p*), is known as "metol."

"Glycine" is *p*-hydroxy-phenylglycine,  $\text{OH.C}_6\text{H}_4\text{NH.CH}_2\text{COOH}$  (*p*); "amidol" is a salt of a *diamino-phenol*.

The dihydroxy- and trihydroxy-benzenes (§§ 303, 305) have a similar reducing action, although not so rapid or energetic; apparently any phenolic or amino-arylic compound, the molecule of which contains two or more phenolic or amino-groups, can be used as a developer in photography (Lumière, 1899).

The aminophenols form numerous derivatives, both as amines and as phenols. When *p*-aminophenol is warmed with ethyl iodide and caustic soda, it is converted into the corresponding phenolic ether, *p*-aminophenetole,  $\text{NH}_2\text{C}_6\text{H}_4\text{OEt}$  (*p*), a crystalline substance of which the acetyl derivative, made by boiling it with glacial acetic acid, is the febrifuge phenacetin.

*p*-Ethoxyacetanilide or *phenacetin*,  $\text{OEt.C}_6\text{H}_4\text{NHAc}$  (*p*), is a crystalline substance melting at  $242^\circ$ ; the physiological properties of acetanilide are much accentuated by the introduction of an ethoxyl-group (compare Cinchonine and Quinine, §§ 399, 400).



**295. The Poly-Nitrophenols: Picric Acid.**—The acidifying influence of nitro-groups is especially evident in *s*-trinitrophenol

or picric acid, which is readily made by adding a somewhat diluted solution of phenol in concentrated sulphuric acid (phenol-sulphonic acid) to concentrated nitric acid. :

After pouring into water, the semi-crystalline product is drained and washed, and finally recrystallised from hot water slightly acidified with sulphuric acid. When the acid is crystallised from benzene, it separates with benzene of crystallisation; benzene "*picrate*,"  $C_6H_5(NO_2)_3 \cdot OH \cdot C_6H_5$ , is a yellow, crystalline substance, which soon loses its benzene by efflorescence; most benzenoid hydrocarbons form such compounds.

Picric acid is also formed by oxidising with potassium ferricyanide the trinitrobenzene formed from *m*-dinitrobenzene; and it is produced by the action of nitric acid on animal tissues and products, such as skin, silk, horn, etc.; it was first made in this manner from silk.

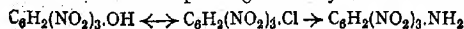
*Trinitrophenol* or *picric acid*,  $C_6H_2(NO_2)_3 \cdot OH$  (Woulfe, 1771), is a bright yellow, bitter, crystalline substance ( $\pi\iota\kappa\rho\varsigma$ =bitter), which melts at  $122^\circ$ , and sublimes when gently heated. It is only sparingly soluble in cold water, but freely in hot water, alcohol and ether, and dyes animal fibres yellow (§ 360).

Aqueous picric acid behaves as a well-defined, monobasic acid, and decomposes alkali carbonates, forming yellow crystalline salts. *Potassium picrate* is scarcely soluble in cold water; the *ammonium salt* is explosive; and the dry *silver* and *lead salts* are very dangerous, and explode when touched. The acid itself can be hammered or melted with comparatively little risk of explosion, but when detonated with mercuric fulminate is decomposed with great violence; it is used as an explosive under the name of "lyddite."

Trinitrophenol itself is colourless, and probably a pseudo-acid (§ 259), the yellow colour being due to ionisation and varying with the solvent. Whilst the aqueous solution is bright yellow, and deposits bright yellow crystals, the solution in concentrated hydrochloric acid yields an almost colourless product, and in non-ionising solvents, such as petroleum or liquid sulphur dioxide, the colour entirely disappears.

Similarly, the crystals gradually lose their colour when dried in a vacuum over concentrated sulphuric acid, whilst the solutions of the alkali picrates, which are fully ionised, are coloured very deeply. It is probable that the picrates, like the nitrophenolic salts, are quinonoid, and derived from a labile *nitroic acid*,  $O \cdot C_6H_2(NO_2)_2 \cdot NO \cdot OH$  (§ 294).

The crystalline *s-trinitrochlorobenzene* or *picryl chloride*,  $C_6H_2(NO_2)_3 \cdot Cl$ , formed by the action of phosphorus pentachloride on picric acid, has the properties of an acid chloride; it is hydrolysed to picric acid by hot hydrochloric acid, and converted into the corresponding amide by ammonia.



↑

C C



*Picramide* or *s-trinitraniline*,  $C_6H_3(NO_2)_3 \cdot NH_2$ , is an orange crystalline substance, melting at  $186^\circ$ , which like acetamide, and unlike aniline, is readily hydrolysed by caustic soda, and reconverted into the hydroxy-compound by nitrous acid, without the intermediate formation of a diazonium compound.

The substituted ammonium picrates are comparatively little soluble in water, and are thrown down as yellow, crystalline precipitates by the addition of picric acid to solutions of aminoid compounds. *Ethylamine*, *n-propylamine* and *urea picrates* are appreciably soluble, but the *tripropylamine* and *aniline salts* are very sparingly so, whilst *alkaloidal picrates*, such as those of pentamethylene diamine, guanidine, creatinine and the vegetable alkaloids, are practically insoluble in water.

As a nitro-compound picric acid is reducible to the corresponding amino-compound, *triaminophenol*,  $C_6H_3(NH_2)_3 \cdot OH$ , an unstable basic substance, which forms stable crystalline salts with mineral acids, and a crystalline *triacetyl derivative* with acetic acid.

Besides picric acid, three other trinitrophenols are known, and there is reason to believe (§ 298) that two more are capable of existence; similarly there should be six dinitrophenols, all of which are known. The trinitrophenols are made by further nitrating the corresponding dinitro-compounds, and these in turn may be prepared either from *o*- or *p*-nitrophenol (although not from the meta-compound, see § 300), or from metadinitrobenzene, etc.

The dinitrophenols resemble both picric acid and the mononitrophenols; they form yellow or red alkali salts, according to their constitution, and when derived from *o*-nitrophenol are volatile with steam. *2:4-Dinitrophenol*,  $C_6H_3(NO_2)_2 \cdot OH(o, p)$  (Laurent, 1841), is a pale yellow, crystalline substance, melting at  $112^\circ$ ,  $K = 0.0080$ ; it is made from phenol or *o*- or *p*-nitrophenol by nitration with somewhat diluted nitro-sulphuric acid.

The remaining isomerides (except the 3:5-compound, which is formed by partially hydrolysing *s*-trinitrobenzene, § 292), are obtained by nitrating *o*- or *p*-nitrophenol with fuming nitric acid, at the ordinary temperature; the 2:6-compound is also formed by oxidising *m*-dinitrobenzene with alkaline ferricyanide (compare Picric acid).

#### THE DINITROPHENOLS.

(See also § 300.)

Constitution.	M.p.	K.	Constitution.	M.p.	K.
2 : 3 ( <i>o, m</i> )	$144^\circ$	0.0012	2 : 6 ( <i>o, o</i> )	$62^\circ$	0.0174
3 : 4 ( <i>m, p</i> )	$134^\circ$	0.0004	2 : 4 ( <i>o, p</i> )	$112^\circ$	0.0080
2 : 5 ( <i>o, m</i> )	$104^\circ$	0.0007	3 : 5 ( <i>m, m</i> )	$122^\circ$	0.001

**296. The Diamine-Benzenes.**—By reducing the dinitrobenzenes or nitranilines with iron and acetic acid, both nitro-groups are attacked, and diaminobenzenes are formed.

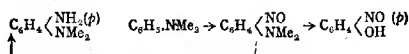
The meta-compound is conveniently made in this way by slowly adding meta-dinitrobenzene to excess of reduced iron suspended in the calculated quantity of very dilute acetic acid, and is extracted from the product with hot water; after evaporation, the semi-crystalline mass may be fractionated in a stream of coal-gas.

*Metaphenylenediamine*,  $C_6H_4(NH_2)_2$  (*m*) (Zinin, 1844), is a colourless, crystalline solid, which melts at  $63^\circ$ , and boils at  $287^\circ$ ; it soon turns brown in the air, from oxidation. It is a diprimary amine, and forms a crystalline *hydrochloride*, but its behaviour with nitrous acid is anomalous, as an intensely brown dye is formed (§ 382); this affords a convenient test for traces of nitrites, such as occur in drinking water.

*Orthophenylenediamine* is a similar crystalline substance, melting at  $102^\circ$ , and is best made from *o*-nitraniline; it is characterised by the red colour, which it forms with ferric chloride in presence of acid. *Paraphenylenediamine* melts at  $147^\circ$ , and is made from aminoazobenzene (§ 381); its dimethyl derivative, *paramino-dimethylaniline*, is made from the corresponding azobenzene derivative, or from *p*-nitroso-dimethylaniline.

Nitrosodimethylaniline is formed by the action of sodium nitrite on a solution of dimethylaniline in dilute hydrochloric acid; the reddish-brown hydrochloride separates at once, and after recrystallisation is decomposed with sodium carbonate solution, the free base being extracted with ether. The nitroso-radical here enters the benzene nucleus.

*Paramitrosodimethylaniline*,  $NO.C_6H_4.NMe_2$  (*p*) (Baeyer, 1894), is a dark green, crystalline substance, melting at  $85^\circ$ . It is hydrolysed by caustic soda to dimethylamine and *paranitrosophenol*,  $NO.C_6H_4.OH$  (a colourless, crystalline substance which forms green solutions), and is reduced by zinc and hydrochloric acid to the corresponding amino-compound, *paramino-dimethylaniline*.



*Paraminodimethylaniline* or *dimethyl-paraphenylenediamine*,  $NH_2.C_6H_4.NMe_2$  (*p*), a crystalline substance melting at  $41^\circ$ , is of technical importance, as it is convertible into various dyes, such as malachite green (§ 366) and methylene blue (§ 365).

The formation of the latter dye, which is a sulphur derivative, constitutes a delicate test for soluble sulphides; its intense blue colour appears on the addition of the diamine hydrochloride and a drop of ferric chloride to the sulphide solution.

**297. Synopsis.**—Benzene forms various poly-substitution products, such as the dinitrobenzenes, the nitranilines, the nitrophenols, and the phenylenediamines. These products fall into three distinct isomeric groups, the *ortho*-, the *meta*-, and the *para*- compounds.



## CHAPTER LIV

### THE ISOMERISM OF THE BENZENE POLY-SUBSTITUTION PRODUCT.

**298. The Ring Formula and Position Isomerism.**—Whilst the three classes of di-derivatives of benzene are derived from one and the same hydrocarbon, the members of the separate classes are not interconvertible. Metadinitrobenzene can be converted into metanitriline and metanitrophenol, but not directly into compounds of the ortho- and para-series. Compounds such as these cannot be metameric, neither can their isomerism be due to any alteration in the nucleus, since they are all derived from the same hydrocarbon; they are therefore position isomerides.

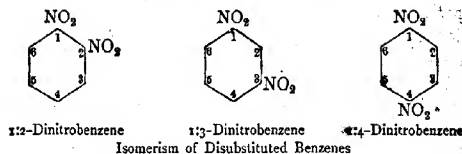
The ring formula accounts in the most thorough manner for the existence of these three sets of products. The formula being symmetrical, the hydrogen atoms occupy equivalent positions, and only one set of mono-derivatives is to be expected. But as soon as a hydrogen atom is replaced by a group or atom of another kind, the symmetry is destroyed, and position isomerism becomes possible.

In nitrobenzene two of the hydrogen atoms (2, 6) are attached to carbon atoms, adjacent to that (1) to which the nitro-group is linked: two others (3, 5) are situated at one remove, whilst the fifth (4) is placed at two removes from this central, nitrated atom.

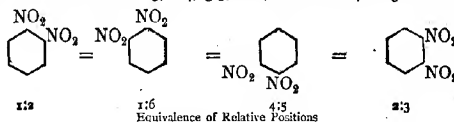


Non-equivalence of Unsubstituted Positions in Nitrobenzene

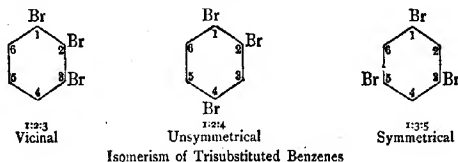
According to the position hypothesis, therefore, the three dinitrobenzenes are represented by the following formulæ.



As the six positions in the formula of the hydrocarbon itself are equivalent, it does not matter where the numbering is started, but it is usual to commence as shown in the figure. It is to be noted that the same position-relations may be represented by other numbers. The 1:2 position is the same as 1:6, 4:5 and 2:3; it is the adjacent position. Similarly, the 1:3 position is the same as 1:5, 2:4, 3:5, etc., and the 1:4 as 3:6 and 2:5.



With regard to the higher substitution products, the same reasoning indicates that there should be three classes of tri-derivatives, and only three (provided that the substituting groups are of the same kind); all conceivable arrangements are reducible to the 1:2:3 or vicinal, 1:2:4 or unsymmetrical, and 1:3:5 or symmetrical positions.



The isomerism of the tetra-derivatives, where such exist, will obviously be the same as that of the di-derivatives, and there will be no isomerism amongst the penta-derivatives or hexa-derivatives.

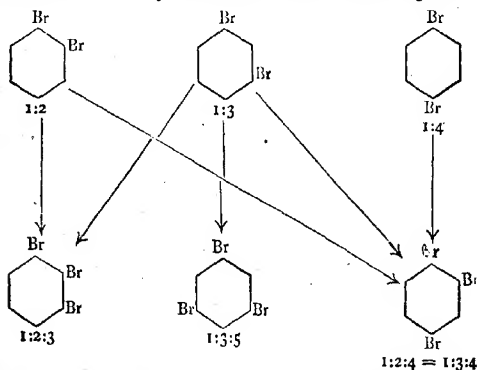
It has been proved experimentally, by somewhat complicated methods, that the six hydrogen atoms in benzene itself are really equivalent, and that in its mono-substitution products, four atoms are arranged in symmetrically disposed pairs, whilst the fifth is unique. But perhaps the most convincing proof of the benzene theory lies in the failure of all attempts to prepare more than one mono-substitution product and three di-substitution products of each kind.

### 299. Orientation of Ortho-, Meta- and Para- Compounds.—The

hypothesis being in line with the facts, it remains to determine which constitution is to be assigned to each of the three known series, or, as it is said, to determine the orientation of the substituted groups. The problem has been solved, amongst other ways, by studying the conversion of the dibromo- into the tribromo-benzenes (Körner, 1874).

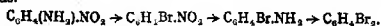
Of the three tribromobenzene formulæ shown above, the vicinal or 1:2:3 formula is derived from the formulæ of 1:2 and 1:3-dibromobenzenes, but not from that of the 1:4-compound; the unsymmetrical or 1:2:4 formula, on the other hand, proceeds from all three modifications; but the symmetrical or 1:3:5 formula can only result from the substitution of bromine in the formula of 1:3-dibromobenzene.

It follows that 1:4-dibromobenzene will yield on bromination only one tribromobenzene, whilst the 1:2 modification will yield two, and the 1:3 modification, three tribromo-products.



Genetic interconnection between the Isomeric Dibromobenzenes and Tribromobenzenes required by the Position Hypothesis.

The three dibromobenzenes are known. The para-compound occurs as a bye-product in the preparation of bromobenzene, but the others are best made from the corresponding nitranilines; these bases are converted into the nitrobromobenzenes by the diazonium interaction; the nitrobromobenzenes are reduced by alcoholic ammonium sulphide (which does not affect the halogen) to the corresponding bromanilines; and these, on further subjection to the diazonium interaction, yield the dibromo-compounds.

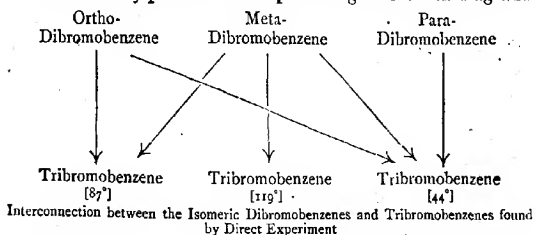


*Paradibromobenzene*, (§ 244), is a colourless, crystalline sub

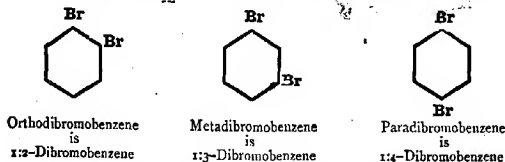
stance, which melts at  $89^{\circ}$  and boils at  $219^{\circ}$ ; and the *ortho*- and *meta*-compounds are heavy liquids boiling at about the same temperature.

When orthodibromobenzene is further brominated, it yields two distinct, crystalline *tribromobenzenes*, melting respectively at  $87^{\circ}$  and  $44^{\circ}$ , whilst from the bromination product of para-dibromobenzene, only the second of these can be obtained. The *meta*-compound on the other hand yields both of these products, and in addition a third crystalline *tribromobenzene*, melting at  $119^{\circ}$ .

These experimental results may be arranged in a diagram, which is exactly parallel to the preceding theoretical diagram.



It follows that in the *ortho*-compound, the bromine atoms occupy the 1:2 position, whilst in the *meta*- and *para*-compounds they assume the 1:3 and 1:4 symmetrical compounds



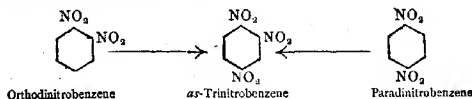
As these three compounds are made from the nitranilines, which are connected genetically with the other di-derivatives, it follows further that in *ortho*-, *meta*-, and *para*-compounds in general, the groups occupy these same positions (Körner, 1874; compare §§ 310, 313, 323).

Many other experimental proofs have been devised. The constitution of *ortho*-compounds follows independently from that of naphthalene (§ 372), and of *meta*-compounds from that of mesitylene (§ 329).

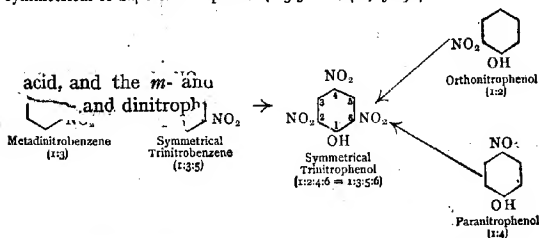
The constitution of the higher derivatives follows in the same way. That of the *tribromo*-compounds is deduced from the above experimental data; the modification of highest melting-point, formed from one only of the *dibromo*-com-

pounds, is 1:3:5 or symmetrical (*s*-) tribromobenzene, whilst that of lowest melting-point, formed from all three dibromo-compounds, is the 1:3:4 or unsymmetrical (*as*-) modification; the tribromo-derivative of intermediate melting-point is therefore 1:2:3 or vicinal (*v*-) tribromobenzene.

Similarly, of the two trinitrobenzenes which are known, that which is formed from both ortho- and para-dinitrobenzenes can only be the 1:2:4 or unsymmetrical modification.



The derivative formed from metadinitrobenzene is therefore either the 1:2:3 or the 1:3:5 variety. It is this trinitrobenzene, however, which can be oxidised to picric acid, which in turn can be made from ortho- and para-nitrophenol, but not from the meta-compound. It follows that the nitro-groups in the acid occupy the ortho- and the para-positions to the hydroxyl; that is to say, they are symmetrically disposed. The second trinitrobenzene is therefore the 1:3:5 or symmetrical modification (the 1:2:3 compound is unknown); and picric acid is symmetrical or 2:4:6 trinitrophenol (1:3:5 = 2:4:6, § 298).



### 300. Position Taken Up by Entering Groups: their Influence.—

Whilst nitrobenzene yields mainly meta- dinitro-benzene, phenol and acetanilide are converted almost exclusively into their para- and orthonitro-derivatives. The same is true of halogen and sulphonic substitution; the substituting radical assumes either the meta-position, or the para- and ortho-positions to the radical already present, but rarely all three.

The rule is not absolutely quantitative, for small quantities of the para- and ortho-compounds often accompany the meta-derivative, and *vice versa*; but the greater part of the action proceeds in the one direction. The para-compound is usually formed in greater quantity than the ortho-modification.



The position taken up is independent of the nature of the substituting group, and depends only on the nature of the group already present. The substituting radical—whether bromine, chlorine, or the nitro- or sulphonic group—takes up the para- (and ortho-) position

when the group already present is

halogen, amidogen, acetamidogen, hydroxyl or methyl;

and

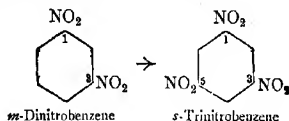
the meta-position

when the group already in position is the

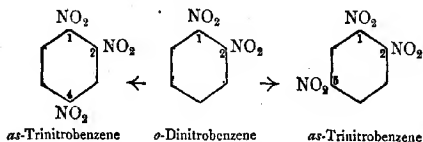
nitro-, sulphonic, carboxyl or aldehyde radical.\*

Thus nitrobenzene yields meta-compounds, whilst bromobenzene yields para- and ortho-derivatives. The rule is well exemplified in the formation of the trinitrobenzenes from the dinitrobenzenes, and of picric acid from phenol.

Metadinitrobenzene gives symmetrical trinitrobenzene, because the 5-position is meta- to both the 1 and the 3 positions.



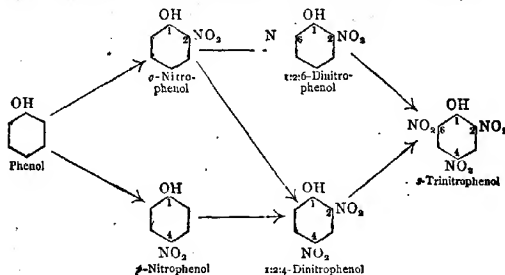
Orthodinitrobenzene gives the unsymmetrical compound, because in both cases the 4 and 5 positions are meta- to one or other of the nitro-groups already present.



Similarly phenol gives in the first place ortho- and para-nitrophenols. These then yield 1:2:4 and 1:2:6 dinitrophenols; the nitro-group in each case takes up the ortho- or para-position with regard to the hydroxyl, and the meta-position with regard to the nitro-group. Finally both dinitro-

\* The rule may be still more concisely stated by saying that if the compound formed by adding a hydrogen atom to the radical already present is readily oxidised ( $\text{H-NO}_2, \text{H-COOH}$ ), the new group takes up the meta-position, whilst if this compound is not readily oxidised ( $\text{H-Cl}, \text{H-OH}$ ) the para- (and ortho-) position is taken up (Crum Brown, 1892).

phenols yield one and the same trinitrophenol, because the new nitro-group again occupies the meta-position with regard to the two other nitro-groups, and the ortho- and para-position with regard to the hydroxyl.



The influence of a substituent group is largely dependent on its position (compare Hydracrylic Acid, § 138). It is greatest in the ortho-, and least in the meta-position, the para-position being intermediate. Metanitriline is the most basic and orthonitriline the least basic of the three nitrilines (§ 293), or in other words, the acidifying influence of the nitro-group is greatest in the ortho-position.

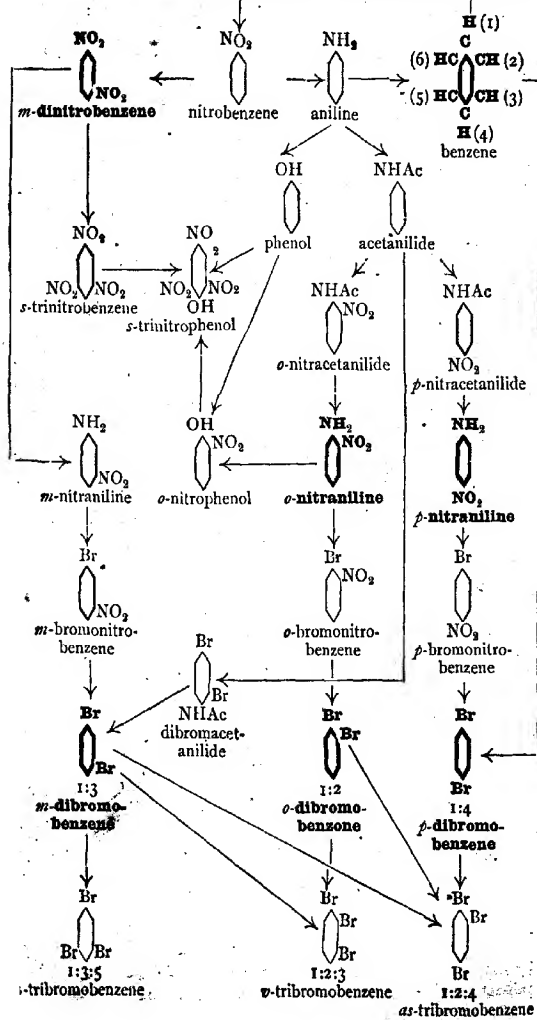
Similarly *o*-nitrophenol and *oo*-dinitrophenol are the most acid, and the *m*- and *mm*-compounds the least acid of the mono- and dinitrophenols (§§ 294, 295), as is shown not only by the relative magnitude of the dissociation constants of these compounds, but also by their general interactions.

These differences are intelligible on stereometric grounds. Ortho-groups being associated with adjacent carbon atoms are separated by the least possible space, whilst meta-groups, which occupy the same relative position as the carboxyl groups of glutaric acid, are the most remote (compare §§ 152, 288). The difference in the remoteness of groups in the meta- and para-positions is well illustrated by the centric stereometric formula of benzenoid compounds (Fig. 24, § 326).

¶ For a similar reason, diortho-substituted benzoic acids (*e.g.* the 2:6-dinitro-acid) cannot be esterified directly, nor can their esters (made from the silver salt), nor their amides or nitriles be hydrolysed. This incapacity is independent of the nature of the substituted groups, and is due to steric hindrance, the molecules of the reagent being unable to approach the carboxyl, etc. (V. Meyer, 1890; compare § 326.)

**301. Synopsis.**—The isomeric substitution-products of benzene are position-isomerides, the groups in the ortho-, meta- and para-compounds occupying the 1 : 2, 1 : 3 and 1 : 4 positions respectively

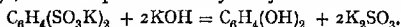
# ISOMERISM OF THE BENZENE POLY-SUBSTITUTION-PRODUCTS



## CHAPTER LV

### THE POLYPHENOLS AND QUINONES

**302. Resorcinol.**—On fusing benzene-*m*-disulphonic acid with potash, both sulphonic groups are replaced by phenolic hydroxyl, and a diphenol or dihydroxybenzene is formed.

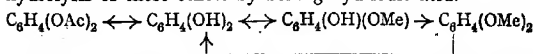


It is isolated in the same way as phenol itself, by extracting the acidified product with ether or amyl alcohol. The same substance is produced by fusing various resins, such as galbanum and asafoetida, with the caustic alkali; it was originally obtained from *m*-iodophenol by the same process.

*Resorcinol* or *m*-*dihydroxybenzene*,  $\text{C}_6\text{H}_4(\text{OH})_2(m)$  (Körner, 1868), is a colourless, crystalline substance, which melts at  $110^\circ$  and boils at  $276^\circ$ ; it is very sweet in taste, and somewhat poisonous, and is freely soluble in water and alcohol; the solubility of phenolic compounds increases with the number of hydroxyl groups in the molecule.

The benzenoid constitution of resorcinol follows from its synthesis, and the presence of two hydroxyl groups in its molecule is proved by its ready conversion into a *diacetate*, boiling at  $278^\circ$ , and a *dibenzoate*, melting at  $117^\circ$ .

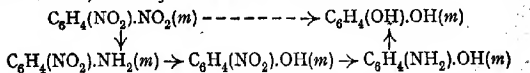
The phenolic character of the groups is demonstrated by its further conversion into *monomethyl* and *dimethyl ethers* by methyl iodide and aqueous potash (§ 254), and by the ready hydrolysis of these ethers by boiling hydriodic acid.



Further the aqueous solution is coloured (dark violet) by ferric chloride (a reaction common to all phenolic compounds), and yields with bromine water a crystalline precipitate of *tribromoresorcinol* similar to tribromophenol.

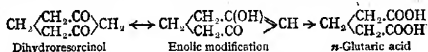
\* *Benzene-*m*-disulphonic acid*,  $\text{C}_6\text{H}_4(\text{SO}_3\text{H})_2(m)$ , is a very deliquescent, crystalline substance, which is formed by heating benzene with fuming sulphuric acid.

The meta-constitution is proved by the formation of resorcinol from *m*-aminophenol (§ 294) by the diazonium interaction, and by its behaviour when reduced.



That resorcinol is a meta-compound would follow from its formation from the metadisulphonic acid, but that it is also formed in this way from the corresponding ortho- and para-compounds; the potash fusion method is therefore of no value as a guide to the relative positions of the groups (compare § 133).

When resorcinol is digested with sodium amalgam in neutral aqueous solution, it is converted into dihydroresorcinol, a compound which forms enolic and ketonic modifications (compare § 144). *Dihydroresorcinol*,  $\text{CH}_2(\text{CH}_2.\text{CO})_2\text{CH}_2$  or  $\text{CO}.\text{C}_6\text{H}_7(\text{OH})$  (Merling, 1893), is a crystalline compound melting at  $106^\circ$ . As an enolic compound, it forms *acetyl* and *benzoyl* derivatives, and reduces alkaline permanganate, yielding *n*-glutaric acid; whilst as a ketonic compound it forms a *dioxime*.



Various alkyl derivatives of dihydroresorcinol can be made synthetically from alkyl sodiomalonates and mesityl oxide (§§ 89, 107), and are similarly resolved by oxidation into alkylglutaric acids, such as  $\beta\beta$ -dimethylglutaric acid (§ 343) and  $\alpha\beta\beta$ -trimethylglutaric acid.

Resorcinol is of technical importance, as when heated with phthalic anhydride it is converted into fluorescein, the mother substance of the eosin dyes (§ 367).

*s*-Methylresorcinol or *orcinol*,  $\text{C}_6\text{H}_3\text{Me}(\text{OH})_2(s)$ , which is a stable, crystalline substance, melting at  $107^\circ$ , is an important constituent of the "litmus" lichens, in which it exists as *orcinol-carboxylic acid*, or its *erythritol ester*. It is also formed synthetically, by condensing diacetylacetone (§ 410) with baryta (Collie, 1893).

**303. Catechol and Quinol.**—The corresponding ortho-compound, pyrocatechin or catechol, occurs in catechu, and was first obtained by distilling this substance; it is best prepared by distilling with hydriodic acid its monomethyl ether, guaiacol, a liquid occurring in quantity in beech-wood-tar.

Catechol may also be made by fusing *o*-phenolsulphonic acid with potash at a low temperature (at a higher temperature resorcinol is formed); it is further produced by distilling protocatecholic acid (§ 310) with lime.

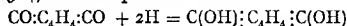
*Catechol* or *o*-dihydroxybenzene,  $\text{C}_6\text{H}_4(\text{OH})_2(o)$  (Reinsch, 1839), is a crystalline substance, resembling resorcinol; it melts at  $104^\circ$ , and boils at  $245^\circ$ .

Its constitution is proved in the same way as that of its

isomeride; as a phenol it forms a coloured *ferric compound*, but the green is turned to violet and red by alkalis; the same reaction is given by its monomethyl ether, *guaiacol* (which still contains a phenolic group), but not by its dimethyl ether, *veratrol*.

As might be anticipated, catechol and its para-isomeride, quinol, are much less stable than the meta-compound; catechol itself is very readily oxidised, and reduces silver in the cold, hence is used as a developer in photography (§ 294); its solution in alkali readily absorbs oxygen from the air, forming dark, resinous products. When oxidised with nitrous acid, the benzene nucleus is broken up, and dihydroxytartaric acid (§ 160) is formed.

Paradihydroxybenzene or quinol was, first obtained by distilling quinic acid (§ 311); it is best prepared by reducing quinone (§ 304) with sulphurous acid.

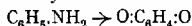


The crude aqueous solution of quinone is saturated with sulphur dioxide, and the quinol extracted from the product with ether; after recrystallisation from hot water containing a little sulphurous acid, it is finally crystallised from hot toluene.

*Quinol* or *hydroquinone*,  $\text{C}_6\text{H}_4(\text{OH})_2(p)$  (Wöhler, 1844), is a crystalline substance, melting at  $169^\circ$ ; unlike its isomerides, it sublimes easily, and is comparatively sparingly soluble in cold water. It is reduced to benzene when distilled with zinc dust, and its para-constitution follows from its relation to quinone.

Like resorcinol and catechol, it forms a *diacetate*, etc., as well as *mono-* and *dimethyl ethers*; it forms a green *ferric compound*, but the colour soon changes to yellow owing to re-oxidation to quinone. Quinol, like catechol, is used as a developer in photography.

**304. Quinone and the Quinones.**—Quinone was originally obtained from quinic acid (§ 311), but is best prepared by oxidising aniline-black with cold chromic acid mixture (Nietzki, 1877). It is also formed from various para-compounds in this manner—from *p*-phenylenediamine, and *p*-aminophenol—and can be made synthetically from succinic acid (§ 306).



Powdered dichromate is slowly added to an ice-cold solution of aniline in dilute sulphuric acid, and in the course of twenty-four hours converts the aniline into aniline-black; a further quantity of dichromate is now added, with the same precautions as before, after which the quinone is extracted with ether and purified by distillation with steam; it may be recrystallised from light petroleum.

As the extraction with ether is peculiarly difficult, owing to the formation

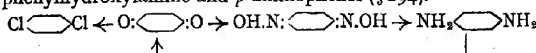
of a persistent emulsion with the black fluid, it saves both time and material to reduce the crude quinone to quinol by saturation with sulphur dioxide; the quinol is then easily extracted with ether, and reoxidised to quinone by boiling with ferric chloride.

**Quinone** or *p*-benzoquinone,  $\text{CO}:(\text{CH}:\text{CH})_2:\text{CO}$  (Woskresensky, 1838), is a golden yellow, volatile, crystalline substance, which melts at  $116^\circ$ , and sublimes freely at a somewhat higher temperature. Its vapour, which is slowly evolved even at ordinary temperatures, possesses a characteristic irritating odour, and attacks the eyes and skin.

Quinone behaves in most respects as a diolefinic diketone; as a diolefin it forms a *tetrabromide*,  $\text{CO}:(\text{CHBr}:\text{CHBr})_2:\text{CO}$ , when brominated in chloroform solution; and although it does not form a hydrazone, it condenses with hydroxylamine to a crystalline *monoxime* and *dioxime*.

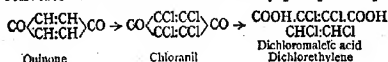
The monoxime, however, is identical with *p*-nitrosophenol (§ 296), and quinone yields on reduction the ditertiary hydroxy-compound, quinol, instead of the secondary alcohol which might be expected; further, it is converted into *p*-dichlorobenzene by phosphorus pentachloride. These anomalies are accounted for by the influence of the benzene nucleus; compounds of the quinone type bear the same relation to the true ketones, as the phenols to the aliphatic and aromatic alcohols.

That quinone is a para-compound is proved by its conversion into *p*-dichlorobenzene by phosphorus pentachloride, and by the reduction of its dioxime to *p*-phenylenediamine; its formation from aniline is probably due to the intervention of phenylhydroxylamine and *p*-aminophenol (§ 294).



Quinone itself has marked oxidising powers; its tetrachloro-derivative, chloranil, which is formed by directly chlorinating it (compare action of bromine), or more conveniently by boiling aniline or phenol with potassium chlorate and hydrochloric acid, is used as an oxidising agent (§ 362).

**Chloranil** or *tetrachloroquinone*,  $\text{CO}:(\text{CCl}:\text{CCl})_2:\text{CO}$ , is a golden-yellow, crystalline substance, which sublimes without melting, and is insoluble in water; the benzene nucleus is here unstable, and the compound is hydrolysed by caustic soda to dichloromaleic acid and dichlorethylene; but it is converted into hexachlorobenzene by phosphorus pentachloride.



When quinol is oxidised or quinone reduced, a dark greenish-brown intermediate compound, *quinhydrone*, is always initially formed, which consists of quinol in ethereal combination with quinone.

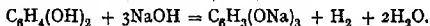
Many homologues of quinone have been prepared by oxi-

dising substituted homologues of aniline, in which the para-position to the amino-group is either unoccupied, or contains a second amino-group or a hydroxyl group. A few ortho-quinones of special type are also known (see also § 373), but meta-quinones are theoretically impossible.

*Triquinone*,  $\text{CO} \cdot \text{C}_6\text{H}_3\text{Me} \cdot \text{CO}$ , is a golden-yellow, volatile, crystalline substance, which melts at  $67^\circ$ , and has the peculiar quinone odour. The three *xyloquinones* (from *o*-, *m*-, and *p*-xylene) are similar.

*o*-Benzoquinone,  $\text{CH} \begin{smallmatrix} \text{CO} \cdot \text{CO} \\ \text{CH} \cdot \text{CH} \end{smallmatrix} \text{CH}$  (Willstätter, 1904), which is made by oxidising catechol with dry silver oxide in ether, differs entirely from the para-quinones; it is a dark red, odourless substance, which is not volatile with steam, and is decomposed when heated.

**305. The Triphenols.**—When resorcinol is fused with caustic soda, hydrogen is evolved violently, and on extracting the acidified solution of the brown melt with ether, phloroglucinol, a crystalline trihydroxybenzene is obtained.

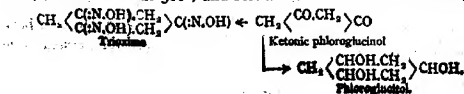


The same substance is obtained in smaller yield by fusing phenol with a large excess of soda; the oxidising action of potash is not nearly as great, and this is why it is used in the synthesis of phenol, and other "alkali fusions." Phloroglucinol was first prepared from the glucoside phloridzin (§ 171), in which it exists in combination with phloretic acid; and it is also formed by fusing various resins with alkali.

*Phloroglucinol* or *s*-trihydroxybenzene,  $\text{C}_6\text{H}_3(\text{OH})_3$  (s) (Hlasiwetz, 1885), is a sweet crystalline substance, which melts at  $218^\circ$ , and sublimes at a somewhat higher temperature.

Its constitution is proved as in the previous cases; it shows the usual properties of a phenol, forms a violet *ferric compound*, and in alkaline solution absorbs oxygen and turns brown; it is convertible into a *triacetate* and a *trimethyl ether*; and its symmetry follows from its conversion into *s*-trichlorobenzene by phosphorus pentachloride.

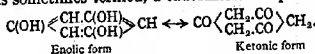
But whilst phloroglucinol is evidently *s*-trihydroxybenzene, it condenses with hydroxylamine, with simple elimination of three molecules of water, to a crystalline *trioxime*,  $\text{C}_6\text{H}_3(\text{N} \cdot \text{OH})_3$ ; it is therefore a triketone as well as a triphenol. Its ketonic character is confirmed by its reduction by sodium amalgam to the corresponding secondary alcohol, *phloroglucitol*,  $\text{C}_6\text{H}_3(\text{OH})_3$ , a sweet, soluble, crystalline substance, which melts at  $184^\circ$ , boils at about  $300^\circ$ , and resembles mannitol in character,



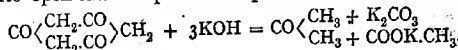
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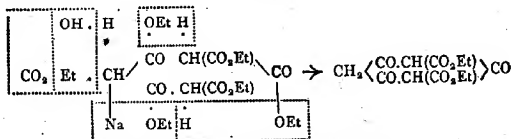
Phloroglucinol, like dihydroroseorcinol and commercial ethyl acetoacetate, is thus a mixture of dynamic isomerides of phenolic and ketonic constitution, or, as it is sometimes termed, a tautomeric compound (§ 144).



When phloroglucinol is chlorinated, it is broken up into dichloroacetic acid and tetrachloroacetone, whilst when it is heated at 160° with strong caustic potash, it is similarly hydrolysed to acetone, acetic acid and carbon dioxide (Combes, 1894); in both cases the aromatic or ring compound is broken up into open-chain aliphatic compounds.



Conversely, on heating ethyl malonate with ethyl sodiomalonate, it condenses to *ethyl phloroglucinol-dicarboxylate*,  $\text{CH}_2[\text{CO} \cdot \text{CH}(\text{CO}_2\text{Et})]_2\text{CO}_2$ , a crystalline substance from which the phenol is readily obtained by fusion with potash (Baeyer, 1885; compare § 146).



Synthesis of Ethyl Phloroglucinol-dicarboxylate.

The consecutive or vicinal trihydroxybenzene is obtained by heating gallic acid (§ 311) at 210°, either alone, or with glycerol or water; it is also formed synthetically by fusing chlorophenol-sulphonic acid with potash.

*Pyrogallol* or *v-trihydroxybenzene*,  $\text{C}_6\text{H}_3(\text{OH})_3$  (*v*) (Scheele, 1786), is a soft, white, crystalline substance, which melts at 132°, and is very soluble in water and alkalis. It is a powerful reducing agent, and hence is used as a developer in photography; its action is much slower than that of the aminoid developers (§ 294). In alkaline solution it absorbs oxygen freely and completely, and is used for this purpose in gas analysis.

As a phenol, pyrogallol forms coloured products with iron salts—a red *ferric*, and a deep blue *ferroso-ferric* compound. Its constitution is proved in a similar manner to that of phloroglucinol.

The third or unsymmetrical trihydroxybenzene is formed by fusing quinol with soda (compare below), in the same way as phloroglucinol from resorcinol. *Hydroxyquinol* or *as-trihydroxybenzene*,  $\text{C}_6\text{H}_3(\text{OH})_3$  (*as*), is a crystalline substance, melting at 132°; it resembles its isomerides in most

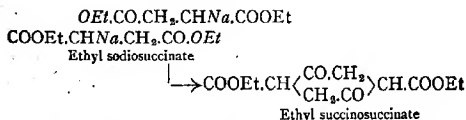
respects, but absorbs oxygen even in aqueous solution, and forms a greenish-brown ferric compound. As hydroxyquinol is derived from a para-compound, it has necessarily the unsymmetrical constitution (compare Tribromobenzenes, § 298).

The three tetraphenols and the pentaphenol required by the ring formula have all been prepared, also the hexaphenol, a compound interesting by reason of its ready synthesis from inorganic materials. *Potassium carbonyl*,  $K_2C_6O_6$ , the explosive compound formed by the direct union of the metal with carbon monoxide in the manufacture of potassium, is the potassium salt of this complex phenol, and is readily converted into it by hydrochloric acid.

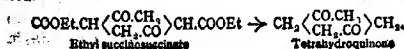
*Hexaphenol* or *hexahydroxybenzene*,  $C_6(OH)_6$  (Nietzki, 1885), is a white substance, which soon oxidises and turns violet in the air. It is converted into a *hexacetate* by acetyl chloride, and is oxidised by nitric acid to the corresponding quinone, *triquinoyl*,  $C_6O_6(+8H_2O)$ , from which it is formed again by reduction with stannous chloride; it is reduced to benzene when distilled with zinc dust.

**306. Reduction Products of the Polyphenols: the Succino-Succinic Synthesis.**—When ethyl succinate is heated with finely divided sodium, the ethyl sodiosuccinate which is initially formed slowly condenses to a ring compound, ethyl succinosuccinate; this compound is a derivative of quinone (compare Phloroglucinol, § 305), and is readily converted into it; and it is also a substituted hexamethylene (§ 287).

The reduced polyphenols and quinones possess all the characteristics of the simpler cycloid alcohols and ketones, and provide additional connecting links between the aliphatic and aromatic compounds. Like the cycloparaffins from which they are derived, they are saturated ring-compounds, and differ from the saturated open-chain compounds only in the saturation of the fourth valencies of the terminal carbon atoms by mutual linkage (§ 288).



*Ethyl succinosuccinate* or *tetrahydroquinone-dicarboxylate*,  $C_6H_8O_6$  ( $COOEt$ )<sub>2</sub> (Hermann, 1882), which after some days can be precipitated from the above product with dilute sulphuric acid, is a colourless or bright-green crystalline substance, melting at 127°; it is readily hydrolysed by dilute acids to tetrahydroquinone, both alcohol and carbon dioxide being eliminated.



*Tetrahydroquinone* or *para-diketohexamethylene*,  $\text{CO}:(\text{CH}_2\text{CH}_2)_2:\text{CO}$  (Hermann, 1882), is a colourless, crystalline substance, melting at  $78^\circ$ ; its intimate relation to quinone is shown by its oxidation to that substance by chromic acid mixture, whilst its constitution as a cycloid aliphatic ketone is equally well demonstrated by its reduction to the corresponding secondary alcohol, *quinitol*, when digested with sodium amalgam in neutral solution.

*Quinitol*,  $\text{CHOH}:(\text{CH}_2\text{CH}_2)_2:\text{CHOH}$  (Baeyer, 1892), is a bitter-sweet, crystalline substance, which melts at  $144^\circ$ , and has the properties of a paraffinoid alcohol (§ 287); when heated with concentrated hydriodic acid it is converted into *p-diiodocyclohexane*,  $\text{CHI}:(\text{CH}_2)_4:\text{CHI}$ , from which cyclohexane (§ 287) was first obtained (Baeyer, 1892).

The penta- and hexa-hydroxy-derivatives of hexamethylene occur in nature; the former is the quercitol of acorns, and the latter the sugar, inositol, which occurs in the heart-muscle of animals, and in unripe French beans and walnut leaves.

*l-Inositol* or *l-hexahydroxycyclohexane*,  $\text{CHOH}:(\text{CHOH})_4:\text{CHOH}$  (Scheerer, 1850), is a sweet crystalline substance, which melts at  $253^\circ$ , and like mannitol can be distilled in a high vacuum.

Although isomeric with, and physically like the hexoses, inositol has little reducing power, and does not form a hydrazone or osazone; nor is it affected by sodium amalgam. The hydroxylic character of its oxygen is proved by its ready conversion into a crystalline *hexacetate* when heated with acetic anhydride and zinc chloride, whilst its ring constitution is proved by its reduction to triiodophenol and benzene when heated with hydriodic acid (Maquenne, 1887); and by its oxidation by concentrated nitric acid to tetrahydroxyquinone.

As an asymmetrical compound, inositol occurs in three stereoisomeric modifications; the active modifications, *d*- and *l*-*inositol*,  $[\alpha]_D = \pm 55^\circ$ , are crystalline substances melting at  $247^\circ$ , which occur naturally in conifers, etc.; when melted together they form *racemic inositol*, melting at  $253^\circ$ .

**307. Synopsis.**—The polyhydroxybenzenes resemble phenol in general character, but are in most cases much more readily oxidised. The paradihydroxy-compound is connected with a ketonic substance, quinone, which differs from the aliphatic ketones in much the same way as the phenols from the alcohols. Many of these substances are synthetically connected, not only with benzene and its derivatives, but also, through hexamethylene compounds, with members of the paraffin group.



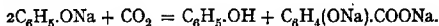
## CHAPTER LVI

### THE PHENOLIC ACIDS

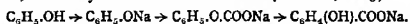
308. **Salicylic Acid and its Aldehyde and Alcohol.**—Several acids are known, which bear the same relation to benzoic acid as the phenols to benzene, and share the characteristics both of the phenols and the carboxylic acids. Some of these occur in nature, and are used in the arts.

Salicylic acid, which is found in the free state in certain species of spiræa, and as an ester (methyl salicylate) in the Canadian wintergreen, is manufactured synthetically from phenol or naphthalene; it was originally obtained by oxidising the corresponding aldehyde.

In the original form of the phenol process (Kolbe, 1874), which is the more convenient in the laboratory, dry, finely-powdered sodium phenate is heated in an oil bath at 200°, and carbon dioxide is passed in under ordinary pressure. Half the phenol is liberated, and distils over, whilst the other half remains as disodium salicylate, from which the acid is set free by hydrochloric acid.



In the technical form of this process, carbon dioxide is forced under pressure, or introduced in the solid form, into a closed vessel containing sodium phenate; on heating the phenyl sodium carbonate thus formed, it is transformed at 140° into sodium salicylate (compare Phenylsulphonamic Acid, § 252). The acid is precipitated from the cold solution by hydrochloric acid, and recrystallised from hot water (Schmitt, 1885).



Salicylic acid is now also manufactured from the corresponding amino-acid, anthranilic acid (§ 273), by the nitrous acid interaction.



The method has been known for many years (Gerland, 1853), but it is only since anthranilic acid has been manufactured from naphthalene, through phthalimide (§ 324), that it has been available as a commercial process.

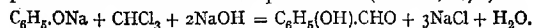
*Salicylic* or *o*-hydroxybenzoic acid,  $C_6H_4(OH).COOH$  (o) (Piria, 1838), is a colourless crystalline substance, of sweetish, but unpleasant, acid taste,  $K=0.102$ ; it melts at  $157^\circ$ , and is freely soluble in hot, but only sparingly in cold water, and is volatile with steam.

The salicylic acid prepared by the carbon dioxide synthesis is liable to contain the isomeric para-hydroxybenzoic acid, especially if the product has been overheated. This is particularly noticeable with potassium phenate (compare Phloroglucinol, § 305); at  $140^\circ$ , the ortho-compound is alone produced, but above this temperature, gradually increasing amounts of the para-compound are formed, until at  $220^\circ$  it is the sole product.

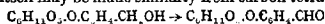
As the physiological properties of the para-acid are different from those of the ortho-compound, natural salicylic acid is usually preferred for medicinal purposes; it is prepared in quantity by the alkaline hydrolysis of oil of winter-green, which consists chiefly of methyl salicylate (Cahours, 1856). The acid prepared from anthranilic acid is practically as pure, however, and salicylic acid may also be purified from small quantities of the para-acid by repeatedly crystallising the mixed lead salts from alcohol, in which lead salicylate is much the less soluble.

*Acetylsalicylic acid* ("aspirin"),  $C_6H_4(OAc).COOH$ , a crystalline substance melting at  $118^\circ$ , which is formed by direct acetylation, is used in medicine in place of the phenolic acid.

The aldehyde of salicylic acid was originally obtained by hydrolysing the glucoside *helicin*, which is formed by oxidising the corresponding alcohol *salicin* (§ 171), the natural glucoside of the willow bark (*salix*). It is made synthetically by boiling phenol with chloroform and aqueous soda (Reimer, 1876).



The oil which separates on acidifying the chloroform product with hydrochloric acid, contains also the isomeric para-compound and unchanged phenol, but the phenol and ortho-aldehyde are alone volatile with steam, and are then separable by means of the crystalline aldehyde-bisulphite. Salicylic acid itself may be made similarly from carbon tetrachloride.



Salicin

Helicin

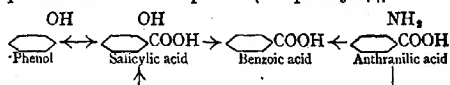
*Salicylic aldehyde*,  $C_6H_4(OH).CHO$  (o), is a colourless, fragrant liquid, which boils at  $196^\circ$ , and stains the skin yellow. It is readily oxidised to the acid by dilute nitric acid, and is resolved by caustic soda into sodium salicylate and the corresponding primary alcohol; as a phenol it forms a coloured (deep violet) *ferric compound*.

*Salicylic alcohol* or *saligenin*,  $C_6H_4(OH).CH_2OH$  (o), which occurs naturally in the glucoside *salicin*, is a crystalline solid, melting at  $82^\circ$ ; it resembles benzyl alcohol in most of its actions, but as a phenol, forms a coloured (violet) *ferric compound*.

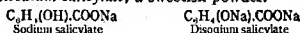
**809. Constitution of Salicylic Acid: Its Isomerides.**—The rela-

tion of salicylic acid to phenol and benzoic acid is shown by many interactions. Not only can it be made from phenol, but it is reconverted into it by distillation with lime; as a phenol, it forms a violet *ferric compound*, which unlike ferric phenate is also formed in alcoholic solution, and is not hydrolysed by acetic acid; like phenol also, it is precipitated by bromine water as a flocculent *tribromo-compound*.

Its carboxylic constitution is established, independently of its relation to benzoic acid, by its interconvertibility with the corresponding aldehyde and alcohol; it is converted into benzoic acid by heating with hydriodic acid, and is formed synthetically, not only through *o*-aminobenzoic acid, which proves its ortho-constitution, but also by fusing *o*-chloro- or *o*-sulphobenzoic acid with potash (compare § 244).

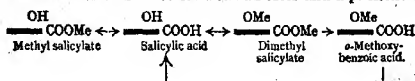


As a carboxylic acid, salicylic acid decomposes sodium carbonate, forming *sodium salicylate*, whilst as a phenol this salt dissolves in caustic soda, forming *disodium salicylate*, a sweetish powder.



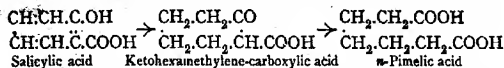
Similarly, it forms two sets of alkyl derivatives. When its methyl-alcoholic solution is treated with hydrogen chloride gas, *methyl salicylate* is formed, identical with the natural ester, whilst when this ester is digested with methyl iodide and dry silver oxide, *dimethyl salicylate* is produced. *Phenyl salicylate* ("salol") is a crystalline substance melting at 43°, which is formed by heating salicylic acid, either alone or with phenol and phosphorus oxychloride. "Betol" is *β-naphthyl salicylate* (§ 371).

The methyl esters are colourless liquids. The first still shows phenolic properties, and is hydrolysed by alkalis to the acid and methyl alcohol; it is therefore an ordinary ester; but the second is no longer phenadic, and is hydrolysed by alkalis to *o*-methoxybenzoic acid ( $K=0.0080$ ), from which the methyl group is removed by boiling with hydriodic acid. The second ester is therefore both an ester and a phenolic ether.



When a solution of salicylic acid in amyl alcohol is digested with metallic sodium, it is reduced to a ketonic cycloid compound (compare § 306), which is then hydrolysed to normal pinelic acid (Einhorn, 1894); this is an interesting instance of the direct conversion of an aromatic compound into an open-

chain compound containing the same number of carbon atoms.

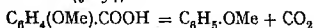


The meta- and para-hydroxybenzoic acids, isomeric with salicylic acid, can be formed from the corresponding amino- and chlorobenzoic acids; the para-acid is also prepared from potassium phenate (§ 308.)

*m-Hydroxybenzoic acid* melts at 200°, and at a higher temperature distils unchanged,  $K=0.0087$ ; *p-hydroxybenzoic acid* melts at 210°,  $K=0.0029$ ; both acids are resolved into phenol when heated with lime, but neither is coloured by ferric chloride, nor is volatile with steam.

*Methyl m-amino-p-hydroxybenzoate* (the antiseptic, "orthoform"), which is a crystalline substance melting at 142°, is made by reducing the corresponding *nitro-ester*; the *nitro-acid* is obtained by nitrating the *p*-hydroxy-acid with dilute nitric acid.

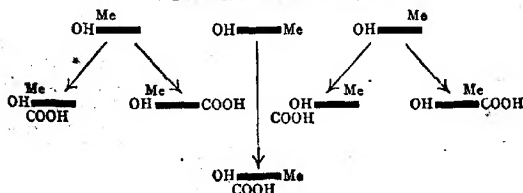
The methyl ether of parahydroxybenzoic acid occurs naturally as *anisic acid*,  $\text{C}_6\text{H}_4(\text{OMe}).\text{COOH}$  (*p*), a crystalline substance, which melts at 185°,  $K=0.0032$ ; like the corresponding ortho-compound it is resolved by heat into carbon dioxide and anisole (§ 254).



Many homologues of salicylic acid and its isomerides are possible. There should be ten *cresotic acids*, and all of these have been made; some of them can be prepared by the carbon dioxide method, or through their aldehydes by the chloroform synthesis. Both of these methods are of very general applicability; *o*- and *m*-cresol each yield two cresotic acids and aldehydes, whilst the *p*-compound yields only one, as the carboxyl or aldehyde group invariably assumes the ortho- or para-position to the phenolic group, and never the meta-position.

The ortho-aldehydes are all volatile with steam, give an intense coloration with ferric chloride and stain the skin yellow. Similar polyhydroxyaldehydes may also be made from catechol, etc. (§ 310).

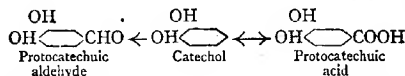
#### THE CRESOLS AND CRESOTIC ACIDS





**310. Protocatechuic Acid and its Derivatives.**—The polyhydroxybenzoic acids, such as protocatechuic and gallic acids, bear the same relation to the polyphenols as salicylic acid to ordinary phenol. Protocatechuic acid occurs, in combination with phloroglucinol, in the mimosa and other plants, and is obtained by fusing catechu, kino and like resins with potash.

*Protocatechuic* or 1:2:4-dihydroxybenzoic acid,  $C_6H_3(OH)_2COOH$  (Stenhouse, 1861), is a crystalline substance, which melts at  $199^\circ$ , and when further heated is decomposed into carbon dioxide and catechol;  $K=0.0033$ . Its constitution as a catechol-carboxylic acid is confirmed by its synthesis, by heating the diphenol with solid ammonium carbonate, and by the synthesis of its aldehyde from catechol.

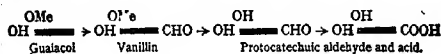


*Protocatechuic aldehyde*,  $C_6H_3(OH)_2CHO$ , which is a very soluble substance melting at  $153^\circ$ , is made synthetically from catechol by the chloroform method (§ 308). *Adrenaline* or *epinephrine*,  $C_9H_7(OH)_2CHOH.CH_2.NHMe$ , the active constituent of the suprarenal gland, which has an extraordinary power of contracting arterioles, and thus arresting hæmorrhage, is a derivative of this substance.

As an ortho-diphenol, protocatechuic acid gives a green coloration with ferric chloride, and, like most of the polyphenols, it reduces silver. As an acid, it forms salts and esters, such as *methyl protocatechuate*,  $C_6H_3(OH)_2COOMe$ , which is a crystalline solid melting at  $224^\circ$ .

The flavouring matter of the vanilla fruit is one of the methyl-protocatechuic aldehydes. *Vanillin*,  $C_6H_3(OH)(OMe).CHO$ , is a crystalline solid, which melts at  $80^\circ$ , and sublimes easily; it has all the properties of an aromatic aldehyde, and is readily converted into the corresponding alcohol and acid—*vanillic acid*—in the usual manner.

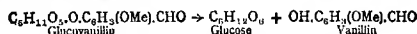
Its constitution is established by its conversion into protocatechuic acid by fusion with potash, and its hydrolysis to methyl chloride and protocatechuic aldehyde by hot concentrated hydrochloric acid. The *para*-position of the phenolic group is determined by the volatility of the compound, as only the parahydroxybenzaldehydes sublime easily.



Vanillin can be synthesised from guaiacol (methylcatechol) by the chloroform method, but is prepared technically from oil of cloves. *Eugenol* or *allyl-guaiacol*,  $OMe.C_6H_3(OH).CH_2.CH:CH_2$ , the principal constituent

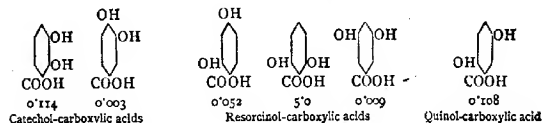
of clove oil, is converted by alcoholic potash into *isoeugenol*,  $\text{OMe.C}_6\text{H}_3(\text{OH}).\text{CH}:\text{CH}.\text{CH}_3$ , which is readily oxidisable to vanillin and acetic acid.

Vanillin is also made technically by similarly oxidising coniferin, the natural glucoside of conifers. *Coniferin*,  $\text{C}_6\text{H}_{11}\text{O}_6.\text{O.C}_6\text{H}_3(\text{OMe}).\text{CH}:\text{CH}.\text{CH}_2\text{OH}$ , which is a crystalline substance melting at  $185^\circ$ , is oxidised by chromic acid mixture to *glucovanillin*, a crystalline aldehyde melting at  $192^\circ$ , and this is hydrolysed by acids or emulsin (§171) to vanillin and glucose (compare §332).



The "heliotrope" perfume, piperonal, which is made technically by oxidising *safrol*,  $\text{CH}_2:\text{O}.\text{C}_6\text{H}_4.\text{CH}_2.\text{CH}:\text{CH}_2$ , the essential constituent of oil of sassafras, is methylene-protocatechuic aldehyde; it may also be made synthetically by the action of methylene iodide on the aldehyde, in presence of alkali (compare §254). *Methyleneprotocatechuic aldehyde* or *piperonal*,  $\text{CH}_2:\text{O}.\text{C}_6\text{H}_3.\text{CHO}$ , is a crystalline substance which melts at  $37^\circ$ , and has a pleasant odour of heliotrope; it is converted into the simpler aldehyde by boiling with concentrated hydrochloric acid.

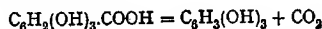
#### D. HYDROXYBENZOIC ACIDS.



There are six dihydroxybenzoic acids, the isomerism of which is identical with that of the dinitrophenols (§295) and nitroxylenes (§323). The strength of these acids is dependent on the relative position of the hydroxyl groups, ortho-groups having far more influence on the activity of the carboxylic hydrogen than similar groups in the para- or meta-positions (compare Nitrophenols); the *oo*-acid is the strongest,  $K=5.0$ , and the *mm*- and *mp* acids the weakest,  $K=0.009$  and  $0.003$ .

**311. Gallie Acid and Tannin.**—The gallic acid from which pyrogallol is obtained is trihydroxybenzoic or pyrogallol-carboxylic acid; it occurs in tea and in oak-galls, and is prepared by hydrolysing tannin with dilute sulphuric acid.

*Gallic acid*,  $\text{C}_6\text{H}_2(\text{OH})_3.\text{COOH}$  (1:3:4:5) (Scheele, 1785), is a white silky, crystalline substance, which is freely soluble in water, and astringent and slightly acid in taste,  $K=0.004$ ; it melts at  $220^\circ$ , and at the same time decomposes into pyrogallol and carbon dioxide.



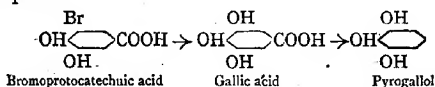
As a phenol, gallic acid forms a black *ferric compound*, which in association with blue colouring matters such as indulines or soluble indigo-derivatives forms the basis of "blue-black"

inks; as a polyphenol it easily reduces silver and gold, and absorbs oxygen in alkaline solution.

The soluble, faintly-colored *ferrous gallate* is quite stable in acid solution, but as the acid is gradually neutralised by the alkali of the paper, it is oxidised to the insoluble ferric compound, and the blue ink becomes permanently black.

When gallic acid is warmed with concentrated sulphuric acid, it is condensed to *rufigallic acid*, a characteristic, insoluble, scarlet compound allied to alizarin (§ 376).

As a triphenol, gallic acid forms a crystalline *triacetyl* derivative, and its constitution as pyrogallol-carboxylic acid is confirmed by its synthesis by fusing bromoprotocatechuic acid with potash.



Gallic acid, like protocatechuic acid, is one of the weakest of its class, owing to the absence of hydroxyl groups in the ortho-position to the carboxyl. The isomeric 1:2:3:4-pyrogallol-carboxylic acid is much stronger ( $K=0.055$ ), and *phloroglucinol-carboxylic acid*, in which two hydroxyl groups are in the ortho-position to the carboxyl, is a powerful acid ( $K=2.1$ ).

The astringency of overdrawn tea and similar vegetable extracts, is due to tannin, a substance which is closely allied to gallic acid; it constitutes about half the weight of oak-galls ("oak-apples").

As it is exceedingly soluble in water, but insoluble in alcohol and ether, it is readily extracted from the powdered galls by shaking them with a mixture of ordinary alcohol and ether. The acid dissolves in the water of the alcohol, and separates as a heavy solution, from which it is reprecipitated on concentration. After several recrystallisations the product becomes colourless.

*Tannin* or *gallotannic acid*,  $\text{C}_{14}\text{H}_{10}\text{O}_9 + 2\text{H}_2\text{O}$ , is a light, amorphous substance, having a very characteristic and not unfragrant odour; it is very soluble, and the solution is intensely astringent. Like gallic acid, tannin forms a black coloration or precipitate with iron salts, which forms the basis of ordinary ink; infusion of galls was used by the Romans to detect the adulteration of verdigris with green vitriol.

Tannin is distinguished from gallic acid by forming a flocculent precipitate with cold gelatine solution (§ 224); it combines in this way with hides and skins,—raw hide completely abstracts the acid from its solution. The complex

compounds thus formed are insoluble in water, and render hide resistant to the latter—leather; the tannic acid from oak-bark is usually employed for this purpose.

The constitution of tannin is proved by its hydrolysis to gallic acid by dilute sulphuric acid, and by its synthesis from this acid by heating it with phosphorus oxychloride. The presence of the five hydroxyl groups is confirmed by the formation of a *pentacetyl derivative*, a crystalline substance melting at  $210^{\circ}$ .

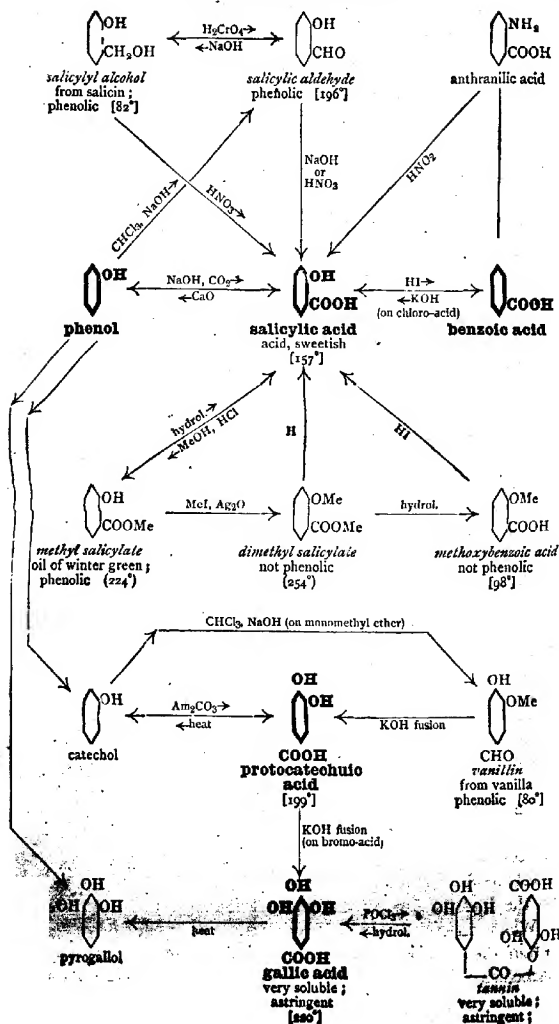


There are many varieties of tannin, such as quercitannic and caffetannic acids; they are mostly derivatives of gallic acid, but in some cases are derived from the corresponding phloroglucinol-carboxylic acid. Many of the tannins occur as glucosides, and are obtained from these by hydrolysis, but gallotannic acid is usually found in the free state.

Various tetra- and pentaphenol-carboxylic acids are known. The crystalline *quinic acid*,  $\text{C}_6\text{H}_7(\text{OH})_4\text{COOH}$ , from which quinone was first obtained, and with which quinine and the related alkaloids are combined in cinchona bark (§ 399), is a tetrahydroxy-hexahydrobenzoic acid; when heated with acetyl chloride and zinc chloride it yields a *tetracetyl* compound melting at  $136^{\circ}$ .

**312. Synopsis.**—The phenolic acids are hydroxy-derivatives of benzoic acid, and act both as carboxylic acids and as phenols. Several of them occur in nature, and are of utility in medicine and the arts. The chief members of the group are salicylic, protocatechuic, gallic, and tannic acids, all of which can be made synthetically.

## THE PHENOLIC ACIDS.



## SECTION XIV

### THE METHYL-BENZENES AND THEIR DERIVATIVES AND ANALOGUES

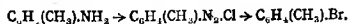
#### CHAPTER LVII'

##### THE CRESOLS AND TOLUIDINES : TOLUENE AS METHYL- BENZENE

**313. The Halogen Toluenes.**—Whilst boiling toluene, in daylight and in absence of a carrier, interacts with halogens as a paraffinoid compound, in the dark, especially when cold and in presence of a carrier, it behaves as a benzene derivative; the nucleal hydrogen atoms are successively replaced, and aromatic substitution is effected.

As the mono-substituted toluenes are di-substitution products of benzene, they exhibit the usual position isomerism, and in accordance with the established rule (§ 300), it is the para- and ortho-compounds which are formed by direct action.

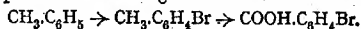
The meta-compounds have to be made indirectly (§ 318), either from aceto-*p*-toluidide or from metatoluidine by the diazonium interaction; in practice all the monohalogen-toluenes are conveniently made by the last method.



The monohalogen-toluenes are colourless, and in some cases crystallisable liquids, which closely resemble the halogen benzenes; unlike the isomeric benzyl compounds they are stable to alkalis, and do not irritate the eyes; they are reduced to the hydrocarbon by sodium in alcohol.

When oxidised with dilute nitric acid these compounds retain their halogen, whilst the methyl is rapidly oxidised to carboxyl. In the *halogen-benzoic acids* thus obtained, the

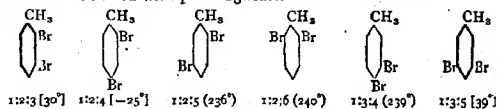
halogen is necessarily in the benzene nucleus; it is therefore similarly placed in the halogen-toluenes.



#### THE ARYL HALOGEN-TOLUENES

	Chloro-		Bromo-		Iodo-	
	M.p.	B.p.	M.p.	B.p.	M.p.	B.p.
Ortho . . .	—	150°	—	180°	—	208°
Meta . . .	—	155°	—	184°	—	212°
Para . . .	-20°	156°	7°	184°	35°	212°

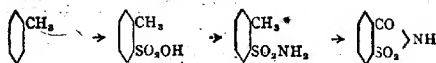
The isomerism of the di-substituted toluenes is more complex than that of the benzene derivatives, as there are not only six distinct dibromocompounds, but also three *bromobenzyl bromides*, isomeric with them. The *dibromotoluenes* are distinguished from one another by their melting and boiling points, and by yielding six distinct crystalline *dibromobenzoic acids* when oxidised with permanganate.



**314. The Toluene-Sulphonic Acids.**—Toluene is sulphonated much more readily than benzene, and the para-compound thus formed is separated from the accompanying ortho-derivative by repeated crystallisation of its barium salt; it is probably formed by isomeric change of the ortho-compound, as the homologous *o*-ethylbenzenesulphonic acid is isomerised to the corresponding para-acid when heated at 100°. The meta-compound is made from aceto-*p*-toluidide (§ 317).

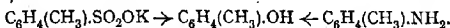
*o*-Toluenesulphonic acid,  $\text{C}_6\text{H}_4(\text{CH}_3)\cdot\text{SO}_3\text{H}$  (*o*) (Terry, 1873), is a well-defined crystalline substance, which resembles the corresponding benzene derivative in all essentials, and forms a *sulphochloride*, and a crystalline *sulphonamide*; it is not attacked by acid oxidising agents, but is converted by alkaline permanganate into the corresponding sulphobenzoic acid (§ 273).

The *meta*- and *para*-sulphonamides are similarly oxidised to the *sulphobenzoic monamides*,  $\text{C}_6\text{H}_4(\text{COOH})\cdot\text{SO}_2\text{NH}_2$ , whilst the ortho-sulphonamide yields, in neutral solution, the imide or internal anide, saccharin (§ 273).



It is to be noted that the meta- and para-acids do not form such internal anhydrides; it is only ortho-groups which interact in this manner. This is accounted for by the ring formula, in which the ortho-groups are attached to adjacent carbon atoms, as in succinic acid, and are therefore physically adjacent.

**315. The Cresols.**—When fused with potash, as in making phenol from benzenesulphonic acid, the toluenesulphonic acids are hydrolysed to the cresols or toluene-phenols. These compounds occur also in coal and beech-wood tars; they can be formed from the corresponding amino-compounds, the toluidines, in the same way as phenol from aniline, and in some cases by other synthetical methods (see *s*-Xylenol, § 322).

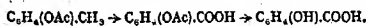


*Ortho*-, *meta*-, and *paracresol*,  $\text{C}_6\text{H}_4(\text{CH}_3)\text{OH}$  (Duclos, 1859), are crystalline substances of high boiling point, which resemble phenol in all essentials. The *ortho*-compound melts at  $31^\circ$ , and gives a blue colour with ferric chloride; the *meta*-compound melts at  $4^\circ$ , and is therefore liquid at ordinary temperatures; whilst the *para*-compound melts at  $36^\circ$ .

The resemblance of the cresols to phenol is very close. Their odour—that of commercial carbolic acid—is not as pleasant, but they are equally good disinfectants and antiseptics. Creasote, the crude mixture of cresols and homologous compounds from wood tar, was formerly used as a meat preservative (*κρέας, σάβω*); it is still used as a disinfectant, and for rendering wood—railway sleepers for example—more durable. The preservative action of wood smoke is largely due to creasote vapour.

The cresols form salts with bases, such as *potassium cresylate*,  $\text{C}_6\text{H}_4\text{Me.OK}$ , and with acids, such as *tolyl sulphate* and *acetate*,  $\text{C}_6\text{H}_4\text{Me.OAc}$ , and they are reduced to toluene when distilled with zinc dust. Unlike the toluenesulphonic acids, they are either not affected by oxidising agents, or else broken up altogether, the methyl groups being to a certain extent protected by the hydroxyl.

When, however, the hydroxyl is combined with acid groups, the methyl can be oxidised to carboxyl in the normal manner. The crystalline *orthotolyl acetate*, formed by the action of acetic anhydride and sodium acetate on the phenol, is converted by chromic acid mixture into salicylic acid.



The cresols are converted by concentrated nitro-sulphuric



acid into *mono*-, *di*- and *tri-nitrocresols*, which are analogous to the nitrophenols and picric acid, and still more intensely coloured.

**316. The Nitrotoluenes.**—Whilst dilute nitric acid only attacks the side-chain of toluene, the hydrocarbon is nitrated by the concentrated acid in the same way as benzene; and as the nitrotoluenes are benzene di-substitution products, they exist in three isomeric forms.

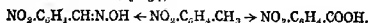
The product of direct nitration, obtained and isolated as in the preparation of nitrobenzene, consists of a mixture of the *ortho*- and *para*-varieties, into which, after washing and drying, it can be resolved by fractional distillation. The *meta*-compound is prepared from aceto-*p*-toluidide (§ 318).

*Ortho*-, *meta*- and *para-nitrotoluene*,  $C_6H_4(CH_3).NO_2$  (Beilstein, 1870), are yellowish liquids, or crystalline solids, which resemble nitrobenzene in odour and chemical character. The *ortho*-compound melts at  $10^\circ$ , and boils at  $218^\circ$ ; the *meta*-compound melts at  $16^\circ$ , and boils at  $230^\circ$ ; whilst the *para*-compound melts only at  $54^\circ$ , and boils at  $238^\circ$ .

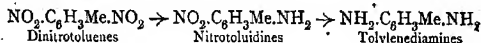
By further nitration, *dinitrotoluenes*, and with difficulty, *trinitrotoluenes*, can be formed, but, as in all such cases, no more than three nitro-groups can be directly introduced into the benzene ring.

The dinitrotoluenes, of which there are six (compare Dibromotoluenes, § 313), are somewhat reactive with alkalis, being partially hydrolysed by aqueous, and converted into phenolic ethers by alcoholic alkalis.

The nitro-group as usual renders the whole molecule more unstable, and not only do these nitro-compounds readily oxidise to the nitrobenzoic acids, but the *ortho*- and *para*-compounds condense with amyl nitrite in presence of sodium ethoxide, forming the corresponding benzaldoximes (compare Isonitrosoacetone, § 234).



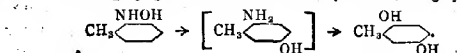
The dinitrotoluenes are reducible to *nitrotoluidines* and *tolylenediamines*, analogous to the corresponding aniline derivatives.



When the nitrotoluenes are cautiously reduced with zinc dust they are converted into the corresponding tolylhydroxylamines, which in turn are oxidisable to the nitrosotoluenes (Bamberger, 1895). The *nitrosotoluenes*,  $C_6H_4.Me.NO$ , are pungent, crystalline substances which like nitrosobenzene and other analogous nitroso-compounds, turn bright green when melted or dissolved.

The *tolylhydroxylamines*,  $C_6H_4.Me.NHOH$ , are unstable crystalline

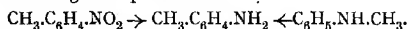
substances which resemble their lower homologue, and are similarly convertible into diazonium and azo-compounds. They are converted by mineral acids into the corresponding *toluquinols*,  $\text{OH} \cdot \text{C}_6\text{H}_3\text{Me} \cdot \text{OH}$ , the *aminocresols*,  $\text{NH}_2 \cdot \text{C}_6\text{H}_3\text{Me} \cdot \text{OH}$ , which are initially formed, being hydrolysed.



**817. The Toluidines.**—By energetic reduction with tin and hydrochloric acid (or technically, with iron and hydrochloric acid), the nitrotoluenes are converted into the corresponding toluidines, or toluene analogues of aniline, of which the para-compound is used extensively in the dye industry. The ortho- and para-compounds are best prepared together from the mixed *o*- and *p*-nitrotoluenes, as they are more readily separated than the latter.

After purifying the mixed bases, as in the preparation of aniline, dilute sulphuric acid is added in amount insufficient to neutralise the whole—fractional neutralisation; the acid combines preferentially with the more basic para-compound, and on distilling the product with steam, the ortho-toluidine alone passes over. Meta-toluidine is made by reducing *m*-nitrotoluene in the usual manner.

Paratoluidine hydrochloride is also formed by isomeric change when methylaniline hydrochloride is heated at  $200^\circ$  (compare Phenylsulphonamic Acid, § 252), and is similarly manufactured by heating aniline hydrochloride with methyl alcohol at a high temperature.



*Ortho*- and *metatoluidine* (Hofmann, 1845) are colourless liquids of high boiling point, resembling aniline in odour, but *paratoluidine* (Hofmann) is a crystalline substance, melting at  $45^\circ$ ; it is noteworthy that in this, as in almost all such cases, the melting point of the para-compound is considerably the higher.

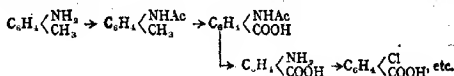
The boiling points of the toluidines are singularly close— $197^\circ$ ,  $199^\circ$ ,  $198^\circ$ , but the three bases are readily distinguished by means of their acetyl compounds, which are prepared by the action of glacial acetic acid or acetyl chloride, in the same way as acetanilide.

*Acetoparatoluidide*,  $\text{CH}_3 \cdot \text{C}_6\text{H}_4 \cdot \text{NHAc}$  (*p*), is a crystalline substance resembling acetanilide, and melting at  $153^\circ$ ; the corresponding ortho- and meta-compounds are similar substances, melting respectively at  $110^\circ$  and  $65^\circ$ .

The toluidines are stronger bases than aniline, but resemble it in character; they are much weaker than the isomeric aliphyl base, benzylamine, in which the amino-group is in the

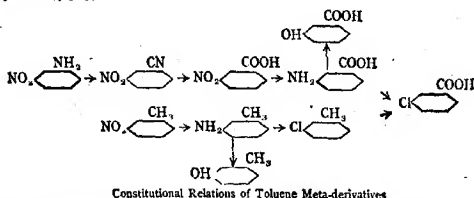
side chain. Like aniline, they are readily convertible by the diazonium interaction into halogen derivatives, etc., and into the hydrocarbon itself, the operations being identical with those already described (§ 260).

Like the cresols, the toluidines are more or less broken up by oxidising agents; *o*-toluidine, for example, forms a blue colouring matter with hypochlorites. But the acetotoluidides, in which the amino-groups are protected, are oxidised by acid permanganate in the normal manner, and the crystalline *acetaminobenzoic acids* thus formed are readily hydrolysed to aminobenzoic acids, from which other substituted benzoic acids can then be obtained.

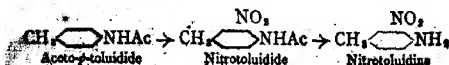


The constitution of the toluidines and their derivatives is readily proved by connecting the bases by means of the diazonium cyanide interaction with the nitranilines, whose constitution is known.

*m*-Chlorobenzoic acid, obtained by the diazonium-cyanide synthesis from *m*-nitraniline, is identical with that which is made from the toluidine prepared from aceto-*p*-toluidide (§ 318); this toluidine and its derivatives are therefore meta-compounds. The same result is obtained with the ortho- and para-compounds, and the constitution of the toluene derivatives is also independently established by their genetic connection with the xylenes (§ 323).

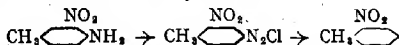


**318. Preparation of Toluene Meta-Derivatives.**—As the toluene meta-substitution products cannot be prepared directly, they are obtained amongst other sources from aceto-*para*-toluidide; this is utilised in the same way as acetanilide in the preparation of *o*- and *p*-nitraniline. The orientation of such compounds is usually indicated in a bracket placed after the formula.



The amino-group being protected by the acetyl, the nitro-group introduced by nitrating the toluidide takes up the ortho-position to the acetamino-group (the para-position is already occupied), and therefore the meta-position to the methyl group; and on hydrolysing this 1:3:4-nitraceto-p-toluidide (which is a crystalline substance resembling the nitracetanilides), the corresponding nitrotoluidine is obtained. The nitration of the toluidines and their derivatives is preceded by the formation of unstable *nitramines*, homologous with phenylnitramine (§ 259).

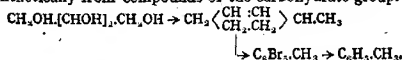
*m*-Nitro-p-toluidine,  $\text{NO}_2 \cdot \text{C}_6\text{H}_3\text{Me} \cdot \text{NH}_2$  ( $\text{Me} : \text{NO}_2 : \text{NH}_2 = 1 : 3 : 4$ ) is a crystalline substance resembling the nitranilines. As its amino-group can be eliminated by the diazonium method (§ 260), it affords a source of metanitrotoluene, and thus of all the meta-derivatives of the hydrocarbon.



*Chlor-aceto-p-toluidide*, *brom-aceto-p-toluidide* and *acetotoluidide-p-sulphonic acid* can be made in the same way, and from these compounds meta-halogen and meta-sulphonic derivatives of toluene may be similarly obtained.

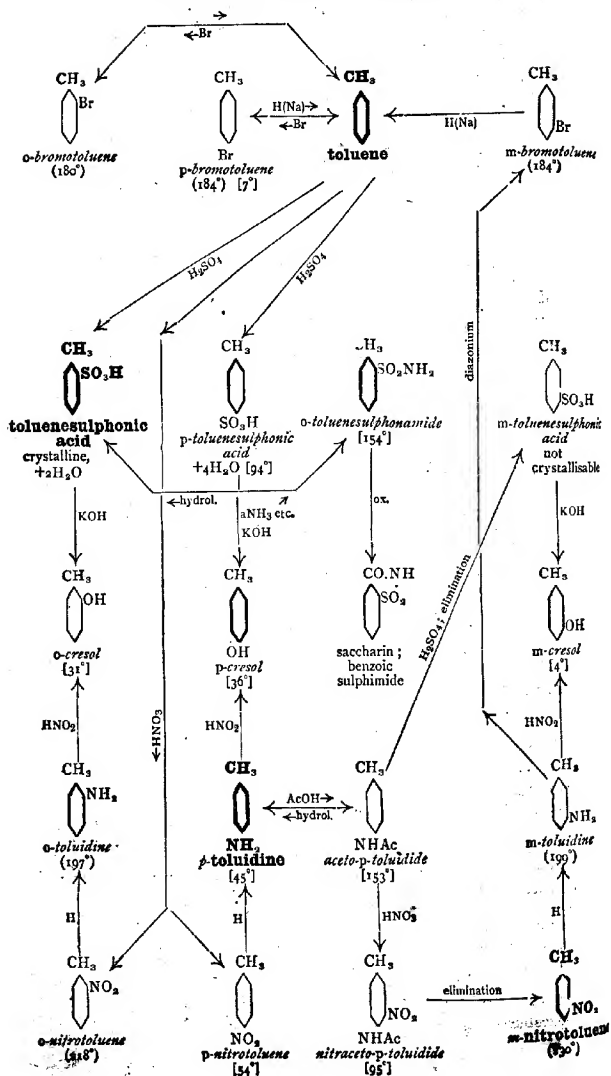
**319. Additive Compounds of Toluene.**—Toluene vapour combines with chlorine in sunlight in the same way as benzene, forming a similar crystalline *hexachloride*. It is also reduced by hydriodic acid, at a high temperature, to *hexahydrotoluene*,  $\text{C}_6\text{H}_{11}\text{CH}_3$ , a liquid of paraffin odour, boiling at  $100^\circ$ , and closely resembling hexahydrobenzene.

The tetrahydrotoluene (compare § 290), which is formed by the successive action of hydriodic and sulphuric acids on perseitol (§ 188), is converted into penta-bromotoluene by prolonged bromination in presence of aluminium bromide. As this bromotoluene is reducible to toluene by sodium and alcohol, the aromatic hydrocarbon may be made synthetically from compounds of the carbohydrate group.



**320. Synopsis.**—The cresols and toluidines are the “aromatic” hydroxy- and amino-derivatives of toluene, corresponding with phenol and aniline. As di-substitution products of benzene, they assume the usual isomeric forms, and the same is true of the related bromo-, nitro-, and sulphonic derivatives.

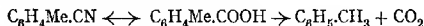
# TOLUENE AS METHYL-BENZENE.



## CHAPTER LVIII

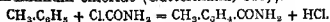
### THE TOLUIC AND PHTHALIC ACIDS AND THE XYLENES

**321. The Toluic Acids.**—The toluic or toluene-carboxylic acids bear the same relation to toluene as benzoic acid to benzene, and physically and chemically closely resemble the lower acid. The nitriles are made from the toluenesulphonic acids and toluidines in the same way as benzonitrile, and are similarly resolved by hydrolysis. The acids are reconverted into the nitriles by distillation with lead thiocyanate, or through the amides, and are resolved into carbon dioxide and toluene when heated with lime.

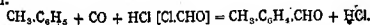


*Paratoluic acid* was originally obtained by oxidising cymene with dilute nitric acid (Noad, 1847), and is also easily prepared from *p*-toluidine by the diazonium cyanide interaction. *Metatoluic acid* can be made from *m*-xylene. *Orthotoluic acid*, which was originally made by a similar process of oxidation, is most readily prepared by boiling phthalide (§ 324) with fuming hydriodic acid and red phosphorus; it can also be made by fusing 1:3-naphthol- or naphthylamine-sulphonic acid (§ 371) with caustic soda.

*p*-Toluamide may be synthesised by the direct interaction of toluene with chloroformamide (§ 192) in carbon disulphide solution, under the influence of aluminium chloride (Gattermann, 1887).



*p*-Toluic aldehyde is formed in a somewhat analogous manner, by passing a mixture of carbon monoxide and dry hydrogen chloride (which behaves as *chloro-formaldehyde*) into ice-cold toluene, containing cuprous and aluminium chlorides (Gattermann, 1897); the complex metallic additive product is decomposed with water, and the aldehyde is distilled with steam, and separated from unchanged toluene by means of its bisulphite compound.



These synthetic processes, like the cyanide synthesis, are of general applicability, and many substituted toluenes may in this manner be con-

verted into the corresponding substituted *p*-toluic acids. The yield with benzene itself is not as good.

Substituted toluic acids may be prepared by direct substitution, but are usually more conveniently made by oxidising the corresponding substituted toluenes. When reduced with sodium in amyl alcohol, the toluic acids are converted into the corresponding *hexahydro*toluic acids, which are saturated cycloparaffinoid compounds homologous with cyclohexanecarboxylic acid (§ 289).

THE TOLUIC ACIDS AND THEIR DERIVATIVES

	Ortho-	Meta-	Para-
Acid . . . . .	[104°]	[109°]	[186°]
Dissociation (K) . . . . .	0.0120	0.0051	0.0051
Chloride . . . . .	(212°)	(214°)	(228°)
Ester . . . . .	(227°)	(228°)	(236°)
Amide . . . . .	[148°]	[94°]	[161°]
Nitrile . . . . .	(205°)	(213°)	[29°]
Hexahydro-acid . . . . .	[102°]	(liquid)	[141°]

**322. The Xylenes:** Xylenol.—The xylenes or dimethyl benzenes,  $C_6H_4(CH_3)_2$  (Fittig, 1870), are light, mobile liquids which resemble benzene and toluene; they are formed with these in the distillation of coal, and accumulate in the fraction of the light oil (§ 243), which boils at about 140°.

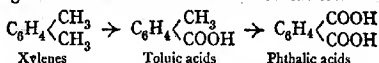
*Orthoxylene*, which boils at 142°, is obtained from *o*-bromotoluene and methyl iodide by the sodium method (§ 279); the yield, however, is very poor.

*Metaxylene*, which boils at 139°, constitutes about three-fourths of the coal-tar fraction, but is difficult to separate from its isomerides on account of the closeness of the boiling points; it may be prepared indirectly by distilling mesitylenic acid (§ 328) with lime, from which its orientation also follows.

*Paraxylene*, which melts at 15° and boils at 138°, is easily made by distilling camphor with anhydrous zinc chloride; it is also formed synthetically, and with good yield, from *p*-dibromobenzene, or *p*-bromotoluene, by the methyl-iodide-sodium method.

That the xylenes are dimethylbenzenes is proved analytically by their successive oxidation to toluic and phthalic acids (§ 324) by appropriate agents; and synthetically, by the direct

formation of the ortho- and para-compounds from the corresponding dibromobenzenes and bromotoluenes.



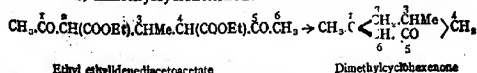
Orthoxylene is completely oxidised to carbon dioxide by chromic acid mixture, as is often the case with ortho-compounds, but it is converted into *o*-toluic acid by dilute nitric acid, and into phthalic acid by alkaline permanganate. Metaxylene is nitrated by concentrated nitric acid, but is oxidised to *m*-toluic acid by moderately dilute nitric acid, and to isophthalic acid by chromic acid. Paraxylene is converted into *p*-toluic and terephthalic acids by dilute nitric acid, and into terephthalic acid by alkaline permanganate.

Like toluene, the xylenes behave as substitution products of both methane and benzene. At the boiling temperature, and in daylight, they yield halogen derivatives, such as the *xylylene chlorides* and *bromides*, which are analogous to the benzyl compounds, and are convertible into similar alcohols, acids, etc.; under ordinary conditions they yield *bromoxylenes*, *nitroxylenes* and *xylene-sulphonic acids*, which with the derived *xylienes* and *xyleneols*, are analogous to the corresponding benzene and toluene substitution-products.

*p*-Xylylene bromide,  $\text{C}_6\text{H}_4(\text{CH}_2\text{Br})_2$ , is a crystalline solid melting at  $143^\circ$ ; the acetate, obtained by boiling it with alcoholic sodium acetate, is quantitatively oxidised to terephthalic acid by alkaline permanganate. 2,4-Xylylene is made technically by isomerisation of dimethylaniline at  $300^\circ$ , *o*- and *p*-toluidine intervening (compare § 317).

Some of these products can also be made synthetically from open-chain compounds. *s*-Xylenol,  $\text{C}_6\text{H}_3\text{Me}_2\text{OH}$  (s), which is a crystalline substance of phenolic character, melting at  $68^\circ$ , is thus prepared from acetaldehyde and ethyl acetoacetate.

In presence of diethylamine or piperidine at a low temperature, these two substances slowly condense to *ethyl ethylidene-diacetoacetate*, CHMe (CHAc.COOEt) $_2$ , a crystalline substance melting at  $80^\circ$ . This acetoacetic derivative is a 1:3-diketone, in which a ketonic group is linked to methyl, and like all such compounds condenses to an unsaturated ring compound when boiled with moderately dilute sulphuric acid; at the same time it loses the carboxyl groups of the acetoacetic ester, thus yielding a cycloolefinic ketone, dimethylcyclohexenone.



*Ethyl ethylidene-diacetoacetate*

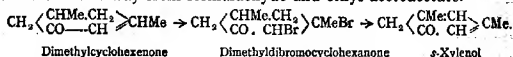
*Dimethylcyclohexenone*

*Dimethylcyclohexenone*,  $\text{CH}_2 \begin{array}{c} \text{CHMe} \cdot \text{CH}_2 \\ \diagup \quad \diagdown \\ \text{CO} \quad \text{CH} \end{array} \text{CMe}$ , a liquid boiling at  $211^\circ$ , is a ketonic derivative of tetrahydroxylene; as an olefine it forms



an additive *dibromide*, an unstable compound which loses its bromine as hydrogen bromide when boiled with glacial acetic acid, and forms the ketonic modification of *s*-xyleneol (Knoevenagel, 1893).

Many such syntheses have been effected; *m*-cresol, for example, may be made in this way from formaldehyde and ethyl acetoacetate.



Dimethylcyclohexenone

Dimethyldibromocyclohexanone

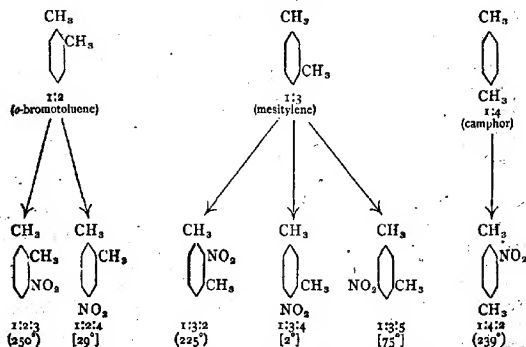
*s*-Xyleneol

Like all phenols the xyleneols are very readily brominated, and in most cases yield *tribromoxyleneols*\* when shaken with bromine water. When these tribromides, or the xyleneols themselves are boiled with bromine and water in an open vessel, they are degraded to the corresponding *tetra-bromocresols*,  $\text{C}_6\text{MeBr}_4\text{OH}$ , and some of these by further degradation, are converted into *pentabromophenol*,  $\text{C}_6\text{Br}_5\text{OH}$ ; in each case a methyl group is eliminated.

**323. Orientation of the Xylenes and Meta-compounds.**—The position of the groups in the xylenes is determined by a method analogous to that employed with the dibromobenzenes (§ 299).

All three xylenes are convertible under the ordinary conditions into mononitro-compounds, of which there are six, constituted similarly to the dibromotoluenes. But whilst the camphor xylene yields only one, the *o*-bromotoluene product gives two, and the xylene from coal tar and mesitylene, three of these products. It follows, as in the former case, that the camphor xylene is the 1:4 or para-compound, and so on.

#### THE SIX MONONITRO-XYLENES



The constitution of metaxylene, and thus of all meta-derivatives of benzene, is confirmed by its preparation from the symmetrical compounds, mesitylenic acid and mesitylene,

### 324<sup>1</sup> Toluic and Phthalic Acids and Xylenes 427

(§ 329), and by the formation of its symmetrical phenol (§ 322) by the acetoacetic synthesis.

These syntheses, taken in conjunction with the nitro-xylene relations, and those of the dibromobenzenes (§ 299), prove that in the syntheses of alkyl-benzenes by the sodium method the alkyl group occupies the same position as the halogen it displaces; the constitution of the higher methylbenzenes is therefore accurately indicated by their synthesis from the various bromobenzenes, etc.

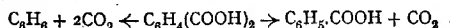
**324. Phthalic Acid and Anhydride.**—The acids which are obtained by further oxidating the xylenes and toluic acids are of both theoretical and technical importance; they are termed the phthalic acids, from the genetic connection of the ortho-compound with the hydrocarbon-naphthalene (§ 372).

*o*-Phthalic (phthalic)<sup>2</sup> acid is made in the laboratory by boiling down naphthalene tetrachloride with excess of concentrated nitric acid; on distilling the residue, the acid anhydride passes over, and is converted into sodium phthalate by boiling with caustic soda.

Phthalic acid is manufactured for technical purposes by oxidising naphthalene with concentrated sulphuric acid containing mercuric sulphate; it is used in large quantities in the dye industry.

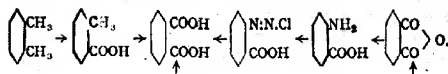
*Phthalic* or *benzene-o-dicarboxylic acid*,  $C_6H_4(COOH)_2$  (*o*) (Laurent, 1836), is a crystalline, sparingly soluble substance, melting at  $213^\circ$ ,  $K=0.121$ ; *phthalic anhydride*,  $C_6H_4(CO)_2O$ , obtained by distilling it, melts at  $128^\circ$ .

That phthalic acid is a benzene-carboxylic acid is proved by its conversion into the hydrocarbon when heated with excess of soda-lime; and that it is a dicarboxylic acid is shown by the conversion of its calcium salt into calcium benzoate when carefully heated at  $230^\circ$  with the calculated quantity of slaked lime.



The molecular formula is independently proved by the vapour density of the esters, such as *ethyl phthalate*; these are liquids of high boiling point, resembling ethyl benzoate, and made in the same manner.

The ortho-constitution of phthalic acid is proved by various syntheses. Not only is it formed by oxidising *o*-xylene and its derivatives with alkaline permanganate (§ 322), but it is produced by hydrolysing the *o*-cyano-benzoic acid, which is prepared from anthranilic acid by the diazonium interaction. Its conversion into an anhydride is also presumptive evidence of an ortho-constitution, as groups in the meta- and para-positions are too remote to interact (§ 288). The complete oxidation of phthalic acid by *chromic acid mixture* is again characteristic of ortho-compounds.



When phthalic anhydride is heated with excess of phosphorus pentachloride at  $200^\circ$ , it is converted into phthalyl chloride, a compound which has the composition, but not the constitution, of a double acid chloride, and is genetically connected with the phthalein dyes (§ 367).

*Phthalyl chloride*,  $\text{C}_6\text{H}_4\langle\begin{array}{|c|} \hline \text{CCl}_2 \\ \hline \text{CO} \\ \hline \end{array}\rangle\text{O}$ , is a crystallisable liquid boiling at  $275^\circ$ ; its unsymmetrical constitution follows from its reduction to a lactic product, phthalide, by zinc and hydrochloric acid, and its synthetic conversion into various substituted phthalides (§ 367).

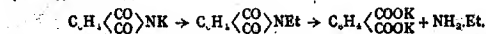
*Phthalide* or *o-hydroxymethyl-benzoic lactone*,  $\text{C}_6\text{H}_4\langle\begin{array}{|c|} \hline \text{CH}_2 \\ \hline \text{CO} \\ \hline \end{array}\rangle\text{O}$ , is a crystalline substance melting at  $83^\circ$ ; it is hydrolysed by alkalis to *o-hydroxymethyl-benzoic acid*, and is reduced to *o-toluic acid* by boiling with hydriodic acid (compare § 151); when boiled with alkaline permanganate it is reoxidised to phthalic acid.

$\text{C}_6\text{H}_4\langle\begin{array}{|c|} \hline \text{CCl}_2 \\ \hline \text{CO} \\ \hline \end{array}\rangle\text{O} \rightarrow \text{C}_6\text{H}_4\langle\begin{array}{|c|} \hline \text{CH}_2 \\ \hline \text{CO} \\ \hline \end{array}\rangle\text{O} \rightarrow \text{C}_6\text{H}_4\langle\begin{array}{|c|} \hline \text{CH OH} \\ \hline \text{COOH} \\ \hline \end{array}\rangle \rightarrow \text{C}_6\text{H}_4\langle\begin{array}{|c|} \hline \text{CH}_2 \\ \hline \text{COOH} \\ \hline \end{array}\rangle$   
 Phthalyl chloride is converted by the more energetic reducing action of sodium amalgam and acetic acid into *phthalyl alcohol*,  $\text{C}_6\text{H}_4(\text{CH}_2\text{OH})_2$ , the double primary alcohol corresponding with phthalic acid; the corresponding double aldehyde, *phthalaldehyde*,  $\text{C}_6\text{H}_4(\text{CHO})_2$ , is obtained by hydrolytically oxidising *o-xylylene bromide* (compare § 322).

Phthalic anhydride is converted by dry ammonia into the corresponding imide; this may also be prepared by simply heating the isomeric *o-cyanobenzoic acid*, or by heating phthalic acid with ammonium thiocyanate (compare Benzonitrile, § 267).

*Phthalimide*,  $\text{C}_6\text{H}_4(\text{CO})_2\text{NH}$  (Laurent, 1842), is a crystalline substance which melts at  $234^\circ$ , and sublimes readily; like succinimide it is a feeble acid.

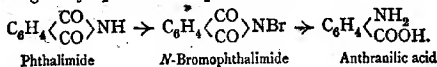
It is converted by alcoholic potash into a crystalline *potassium salt*, the metal of which is readily exchanged for alkyl and substituted alkyl groups, when heated in alcoholic solution with alkyl iodides, etc.; the products thus obtained readily yield primary amines and amino-acids when hydrolysed (§§ 212, 217).



When sodium phthalimide is warmed with a hypochlorite it is converted into anthranilic acid, an unstable *nitrogen halogen compound* (§ 212) intervening (Hoogewerf, 1892);

325] *Toluic and Phthalic Acids and the Xylenes* 429

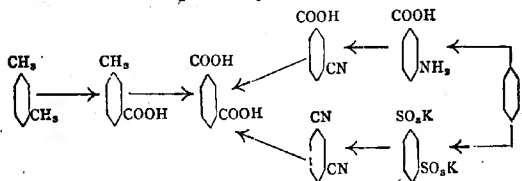
anthranilic acid (§ 273) is thus manufactured technically from the coal-gas bye-product, naphthalene.



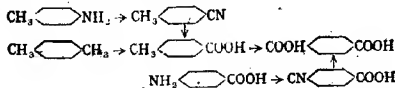
**325. Isophthalic and Terephthalic Acids.**—The isomeric meta- or isophthalic acid which is formed by boiling *m*-xylene or *m*-toluic acid with chromic acid mixture, can also be synthesised from *m*-cyanobenzoic acid and *m*-dicyanobenzene; it is further obtained in small amount when acetaldehyde-resin (§ 85) is oxidised with nitric acid.

*Isophthalic* or *m*-*phthalic* acid,  $\text{C}_6\text{H}_4(\text{COOH})_2$  (*m*) (Fittig, 1868), is a crystalline substance, which is sparingly soluble, even in boiling water, and separates in fine needles on cooling the solution; it melts at above  $300^\circ$ , and then sublimes unchanged, without forming an anhydride;  $K=0.0287$ .

When distilled with soda-lime, it yields benzene, and its meta-constitution is proved by the above cyanide syntheses.



The third benzene-dicarboxylic acid, terephthalic acid, is formed when para-xylene, or any para-dialkyl derivative of benzene is oxidised; it is thus prepared from *p*-xylylene bromide (§ 322), and from the sodium *p*-toluate, made from *p*-toluidine; it can also be made from paramino-benzoic acid by the diazonium cyanide synthesis. Its constitution follows from these various synthetic relations.



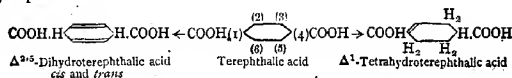
The permanganate solution is added to the boiling dilute solution of the toluate until it ceases to be decolorised, and after filtering off precipitated manganese dioxide, the terephthalic acid is precipitated from the hot product with hydrochloric acid. With the xylene compound the procedure is similar, except that alkaline permanganate is employed.

*Terephthalic* or *p-phthalic acid*,  $C_6H_4(COOH)_2$  (*p*) (Caillot, 1847), is a microcrystalline substance, which is sharply distinguished from its isomerides by its insolubility in water, alcohol and ether, and by subliming without melting or forming an anhydride.

**326. The Reduced Phthalic Acids.**—When cold aqueous terephthalic acid is digested with sodium amalgam, it is reduced to a dihydro-acid, whilst when the solution is boiled and kept strongly alkaline during the reduction a tetrahydro-acid is formed. By treatment with water and alkalis under various conditions these reduction products are convertible into isomeric acids, and by further reducing the tetrahydro-acids with hydriodic acid the corresponding hexahydro-acid is obtained (Baeyer, 1886–1889); this may also be made by the malonic synthesis.

There are ten of these reduced terephthalic acids, namely five dihydro-, three tetrahydro-, and two hexahydro-compounds; their isomerism depends partly on the varying position of the olefine linkages, and partly on the formation of stereoisomerides of the maleic and fumaric type.

The isomerides are named according to the position of the olefine linkage or linkages ( $\Delta$ ): thus in  $\Delta^{2,6}$ -dihydroterephthalic acid the double bonds are between carbon atoms 2 and 3, and 5 and 6 respectively, and in  $\Delta^1$ -tetrahydroterephthalic acid, the double bond is between carbon atoms 1 and 2; the numbering in each case starts from one of the carboxyl groups.



Stereoisomerism is only possible in those acids in which both carbon atoms to which carboxyl groups are attached are saturated. It will be seen from the tetrahedral models (Fig. 24) that in such case the carboxyl groups may be either on the same or on opposite sides of the ring-plane; but in the centric formula for terephthalic acid, as represented stereometrically, the fourth valencies are on the same side of this plane, and stereoisomerism is impossible.

The preparation of these stereoisomeric reduction-products is therefore very strong evidence for the centric constitution of benzenoid compounds (Baeyer, 1889).

The *dihydroterephthalic acids*,  $\text{COOH.C}_6\text{H}_4\text{COOH}$ , vary considerably in stability. Their olefinic constitution is shown

by their ready additive combination with bromine and hydrogen bromide, and their rapid reduction of cold dilute alkaline permanganate.

The  $\Delta^{1,4}$ -acid (see diagram, p. 432), which is the most stable, is formed by reducing terephthalic acid with sodium amalgam in cold alkaline solution, and by the action of alkalis on the other dihydro-acids; as an olefinic compound it is broken up by hot alkaline permanganate, but it is reconverted into terephthalic acid by alkaline ferricyanide.

The  $\Delta^{2,5}$ -acid, which is made by reducing terephthalic acid in ice-cold neutral solution, occurs in two modifications, a moderately soluble *fumaroid* form, and a readily soluble *malzoid* form. The  $\Delta^{1,3}$ -acid is made by debrominating the dibromo-hexahydro-acid with alcoholic potash, and the  $\Delta^{1,5}$ -acid is obtained by boiling the  $\Delta^{2,5}$ -acid with water.

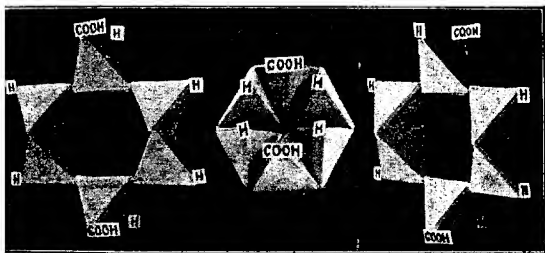


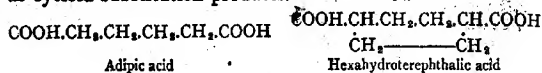
Fig. 24.—Stereoisomerism of Cyclic Compounds.  
Centric Formula of Benzenoid Compounds represented Stereometrically.  
*Cis*- $\Delta^{2,5}$ -Dihydroterephthalic acid      Terephthalic acid      *Trans*- $\Delta^{2,5}$ -Dihydroterephthalic acid

The *tetrahydroterephthalic acids*,  $\text{COOH.C}_6\text{H}_8\text{.COOH}$ , are monolefinic compounds, and like the dihydro-acids readily combine with bromine and hydrogen bromide, and reduce cold, dilute alkaline permanganate.

The more stable  $\Delta^1$ -acid, a readily soluble, crystalline substance, which melts at above  $300^\circ$  and sublimates easily, is made by reducing terephthalic acid, or the  $\Delta^{1,4}$ -dihydro-acid, with sodium amalgam in boiling alkaline solution. The  $\Delta^2$ -acid is made by reducing the  $\Delta^{1,3}$  or  $\Delta^{1,5}$ -dihydro-acids in the cold, and is converted into the  $\Delta^1$ -tetrahydro-acid by alkalis; it forms two stereometric modifications, a sparingly soluble *trans*-acid, melting at  $220^\circ$ , and a more soluble *cis*-acid melting at  $155^\circ$ .

The stereoisomeric (*cis* and *trans*) hexahydroterephthalic acids,  $\text{COOH.C}_6\text{H}_{10}\text{.COOH}$ , are saturated compounds; they have no action on cold, dilute alkaline permanganate, and when brominated yield substitution products, in the same way as an aliphatic dicarboxylic acid. Their properties are very

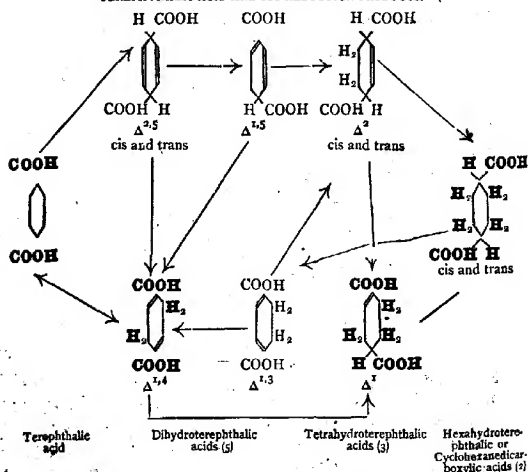
similar to those of adipic acid, of which they may be regarded as cycloid substitution products.



The acid which is made by reducing the  $\Delta^1$ -tetrahydro-acid with hydriodic acid, or synthetically, forms two modifications, which may also be prepared independently by reducing the stereoisomeric bromohexahydro-acids,  $\text{COOH} \cdot \text{C}_6\text{H}_9\text{Br} \cdot \text{COOH}$ . The latter are formed by the addition of hydrogen bromide to the  $\Delta^1$ -tetrahydro-acid; the less soluble bromo-acid yields the fumaroid hexahydro-acid, whilst the more soluble acid from the mother-liquor gives its maléoid isomeride.

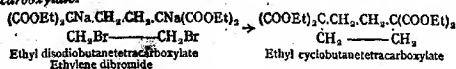
Trans-hexahydroterephthalic acid,  $\text{COOH} \cdot \text{H} \rangle \text{C}_6\text{H}_8 \langle \text{COOH}$ , is sparingly soluble in water, and insoluble in chloroform; it melts at  $295^\circ$ , and sublimes readily. The corresponding cis-acid,  $\text{COOH} \cdot \text{H} \rangle \text{C}_6\text{H}_8 \langle \text{COOH}$ , is very soluble in water, and soluble in chloroform; it melts at  $162^\circ$ , and when heated with hydrochloric acid at  $180^\circ$  is converted into the trans-acid.

TEREPHTHALIC ACID AND ITS REDUCTION PRODUCTS.

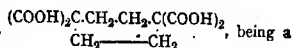


Trans-hexahydroterephthalic acid can be synthesised from ethylene bromide and ethyl sodiomalonate. When an excess of sodium is used in the synthesis of trimethylene derivatives (§ 289), the ethylene bromide combines with two molecules of the malonate, forming ethyl butane-tetracarboxylate,  $(\text{COOEt})_2\text{CH} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}(\text{COOEt})_2$ . This compound, as a

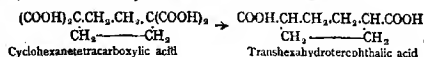
substituted double malonic ester, forms a *disodium derivative*, which again combines with a molecule of the bromide, giving *ethyl cyclohexane tetracarboxylate*.



*Cyclohexanetetracarboxylic acid*,

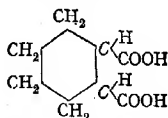


substituted malonic acid, decomposes when heated, yielding carbon dioxide and a cyclohexane-dicarboxylic acid; this is identical with transhexahydroterephthalic acid (Perkin, jun., 1892). As the reduced acid is oxidised to terephthalic acid when heated at 300° with the calculated amount of bromine, an additional synthesis of the latter is afforded.



The reduction products of terephthalic acid have no longer the character of benzene derivatives; the dihydro-acids and tetrahydro-acids behave as unsaturated olefinic compounds, whilst the hexahydro-acids, like other cycloparaffinoid products, resemble the aliphatic compounds in behaviour.

Similar sets of isomeric acids are obtained by reducing phthalic and isophthalic acids, and in the case of the ortho-compounds there are still further possibilities of isomerism. *Transhexahydrophthalic acid*, a crystalline substance melting at 221°, is asymmetrical in constitution, and can be resolved by the alkaloidal (quinine) fractionation (§ 139) into optically active isomerides ( $[\alpha]_D = \pm 18^\circ$ ), melting at about 180°.

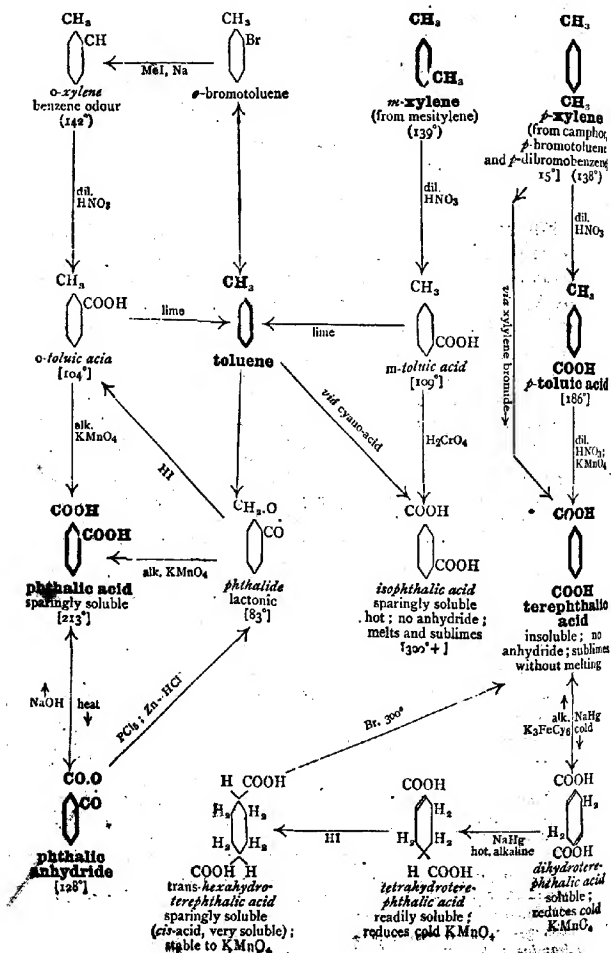


Transhexahydrophthalic acid.

**327. Synopsis.**—The toluic and phthalic acids are oxidation products of the xylenes or dimethylbenzenes, and like these show the usual triple isomerism. When reduced, they are converted into unsaturated, cyclo-olefinic and saturated, cycloparaffinoid products, some of which can be made synthetically from open-chain compounds; the reduced phthalic acids exist in many isomeric forms.



## THE TOLUIC AND PHTHALIC ACIDS AND THE XYLENES.

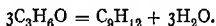


## CHAPTER LIX

### THE POLYMETHYL-BENZENES

**328. Mesitylene.**—According to the ring formula, there should be three trimethylbenzenes, three tetramethylbenzenes, one pentamethyl and one hexamethyl compound. All of these are known; two of the trimethyl-compounds, pseudocumene and mesitylene, and one of the tetramethyl-compounds, durene, are formed in coal distillation.

The most important of the polymethylbenzenes is mesitylene, the symmetrical trimethyl-compound, which is made synthetically by condensation of acetone.



Mesitylene can be isolated from the higher fraction of the light oil of coal tar, but is more easily prepared from acetone, and was first obtained in this way. The acetone, diffused through a quantity of dry sand, to prevent frothing, and to moderate the action, is mixed with moderately concentrated sulphuric acid, and on distilling the product after a day or two, the hydrocarbon passes over, accompanied by water and a little unchanged acetone. The yellow oil which floats on the water is dried and fractionated.

*Mesitylene* or *s-trimethylbenzene*,  $\text{C}_6\text{H}_3\text{Me}_3$  (s) (Kane, 1838), is a colourless, aromatic, highly refractive liquid, which boils at  $163^\circ$ , and freezes at  $-60^\circ$ . Although formed from acetone by simple condensation, its aromatic character is at once suggested by the ease with which it is brominated, sulphonated and nitrated.

*Nitromesitylene*,  $\text{C}_6\text{H}_2\text{Me}_3\text{NO}_2$  (s), is a crystalline compound melting at  $142^\circ$ ; when reduced with tin and hydrochloric acid it is converted into aminomesitylene or *mesidine*,  $\text{C}_6\text{H}_2\text{Me}_3\text{NH}_2$  (s), an oily liquid, which is converted by the diazonium interaction into the corresponding phenol, *mesitol*,  $\text{C}_6\text{H}_2\text{Me}_3\text{OH}$  (s), a stable crystalline substance.

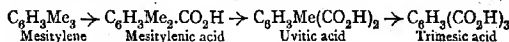
*Mesidine* is a more active compound than aniline; it is readily methylated to *dimethylmesidine*,  $\text{C}_6\text{H}_2\text{Me}_3\text{NMe}_2$  (s), which when nitrated exchanges an amino-methyl group for nitroxyl, yielding a crystalline *nitramine*,  $\text{C}_6\text{Me}_3(\text{NO}_2)_2\text{NMe}\cdot\text{NO}_2$  (Klobbie, 1888).

*Nitrosomesitylene*,  $\text{C}_6\text{H}_2\text{Me}_3\text{NO}$  (s), is distinguished from the lower

nitroso-compounds (§§ 263, 316) by forming a colourless solution in cold benzene, the molecules in which are found by the cryoscopic method to be double; the unassociated nitroso-compounds are therefore green.

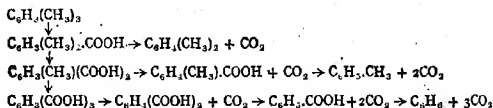
The benzenoid constitution of mesitylene is proved by its oxidation to various benzene-carboxylic acids. The hydrocarbon gradually dissolves when boiled in a reflux apparatus with dilute nitric acid, yielding two difficultly soluble acids, mesitylenic acid and uvitic acid, of which the latter is volatile with steam. By oxidation with chromic acid mixture, uvitic acid is converted into trimesic or benzenetricarboxylic acid, which cannot be further oxidised without breaking up.

Mesitylene is therefore a trimethylbenzene, the three acids being formed by successive oxidation of the methyl groups (Pittig, 1867).

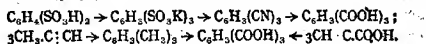


*Mesitylenic* or *s-dimethylbenzoic acid*,  $\text{C}_6\text{H}_3\text{Me}_2\text{COOH}$ , a crystalline substance melting at  $166^\circ$ , is a monobasic acid, and when distilled with lime is converted into *m*-xylene, so that it is a carboxylic acid of this hydrocarbon. *Uvitic* or *s-methylisophthalic acid*,  $\text{C}_6\text{H}_3\text{Me}(\text{COOH})_2$ , which melts at  $288^\circ$ , is a dibasic acid, and on similar treatment yields either *m*-toluic acid or toluene, according to the proportion of alkali; it is thus a toluene-dicarboxylic acid.

*Trimesic acid*,  $\text{C}_6\text{H}_3(\text{COOH})_3$ , which melts at  $300^\circ$  and sublimes readily, is a tribasic acid; under the same conditions it yields either isophthalic acid, benzoic acid, or benzene, and is thus a benzenetricarboxylic acid.



The above result is confirmed by the synthesis of trimesic acid from benzene-trisulphonic acid by the cyanide method, and by that of mesitylene and trimesic acid from allylene and propiolic acid by polymerisation. Uvitic acid is also formed in an analogous manner by the action of baryta on pyruvic acid (§ 137).

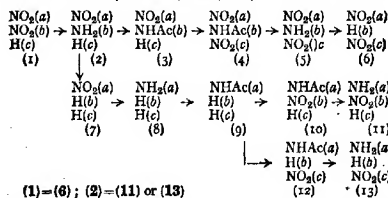


**329. Orientation of Mesitylene and Meta-Compounds.**—The synthesis of mesitylene by condensation of acetone renders it probable that it is a symmetrical compound, for there is no reason to believe that the condensing molecules behave in different ways, as would have to be the case to produce an unsymmetrical product (Baeyer, 1867). This, however, is not a rigid proof, for benzene hexachloride, which is necessarily

symmetrical, yields, when heated, *as*-trichlorobenzene.

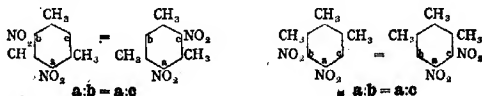
A complete proof of the symmetry of mesitylene is afforded by a study of its dinitro- and nitro-amino-derivatives. Although there are three replaceable hydrogen atoms (*a*, *b*, *c*) in the benzene nucleus, if mesitylene is a symmetrical compound there can be only one dinitro-, and one nitro-amino-derivative. Now only one *dinitromesitylene* and one *nitroaminomesitylene* are known, and more than this, each can be so prepared that these groups occupy different positions, whilst the substances remain unaltered; i.e.  $a=b=c$ .

The dinitromesitylene (1), in which the groups occupy the positions (say) *a*, *b*, can be converted by the stages indicated into a second dinitro-compound (6), in which, whilst one of the groups retains its original position (*a*), the other takes up the third available position (*c*). But the actual substances are identical, and so, therefore, are their formulae—(1)=(6).

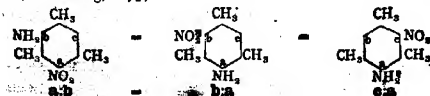


(1)=(6); (2)=(11) or (13)

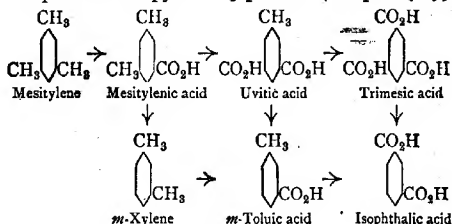
The positions *b* and *c* are therefore similarly situated with regard to *a*, that is, they are both ortho or meta to the *a* position (they cannot both be para). This result is in harmony with either the symmetrical or the vicinal formula for trimethylbenzene, but is irreconcilable with the asymmetrical formula.



The nitroaminomesitylene (2), formed by partial reduction of the dinitro-compound (1), can be converted by a similar process into a second nitro-amino-compound (11) or (13), in which the amino-group now occupies the position *a*, whilst the new nitro-group takes up the position *b* or *c*. But the two substances (2) and (11) or (13) are again identical, and whether the new nitro-group is at *b* or at *c* (it must be in one or the other of these positions), this second result is consistent only with the symmetrical formula (Ladenburg, 1875).

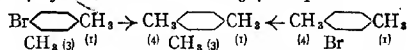


As mesitylene is symmetrical or 1:3:5 trimethylbenzene, the xylene and meta-toluic and isophthalic acids obtained from it must be 1:3 compounds; that is, the groups in the meta-compounds occupy the 1:3 position (compare § 299).



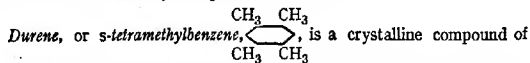
**330. The Higher Methyl Benzenes.**—Of the two trimethylbenzenes isomeric with mesitylene, the unsymmetrical compound, pseudocumene, occurs, as already indicated, in considerable quantity in coal-tar oil.

*Pseudocumene* or *as-trimethylbenzene*,  $\text{C}_6\text{H}_3\text{Me}_3$  (*as*), is a liquid which resembles mesitylene, and boils at  $170^\circ$ . Its constitution and orientation are proved by two direct syntheses from bromo-*p*-xylene and bromo-*m*-xylene by the methyl-iodide-sodium method; and as it is derived from both 1:3 and 1:4-xylene, it must be a 1:3:4-compound.



The vicinal compound, *hemimellitene*,  $\text{C}_6\text{H}_3\text{Me}_3$  (*v*), is a similar liquid, boiling at  $175^\circ$ .

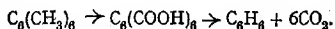
Of the three tetramethylbenzenes, the symmetrical compound, *durene*, occurs with the trimethyl-compounds in coal tar.



campbor odour, melting at  $79^\circ$ ; its constitution follows from its synthesis from dibromoxylene and methyl iodide by the sodium method (compare § 323), and from its oxidation to symmetrical dimethylisophthalic and dimethylterephthalic acids. *Durene* can also be made from hexamethylbenzene.

*Hexamethylbenzene* can be synthesised both from benzene and methyl chloride by the aluminium chloride method, and from crotonylene by polymerisation. Most of the intermediate polymethylbenzenes can be made by the aluminium chloride method, but as it is difficult to stop the action at a definite intermediate point, mixtures are usually obtained.

*Hexamethylbenzene* or *mellithene*,  $C_6(CH_3)_6$ , is a crystalline substance, melting at  $164^\circ$ . It is oxidised by potassium permanganate in the normal manner to *mellitic* or *benzene-hexacarboxylic acid*,  $C_6(COOH)_6$ , a soluble, crystalline substance which is converted into benzene when heated with excess of lime.

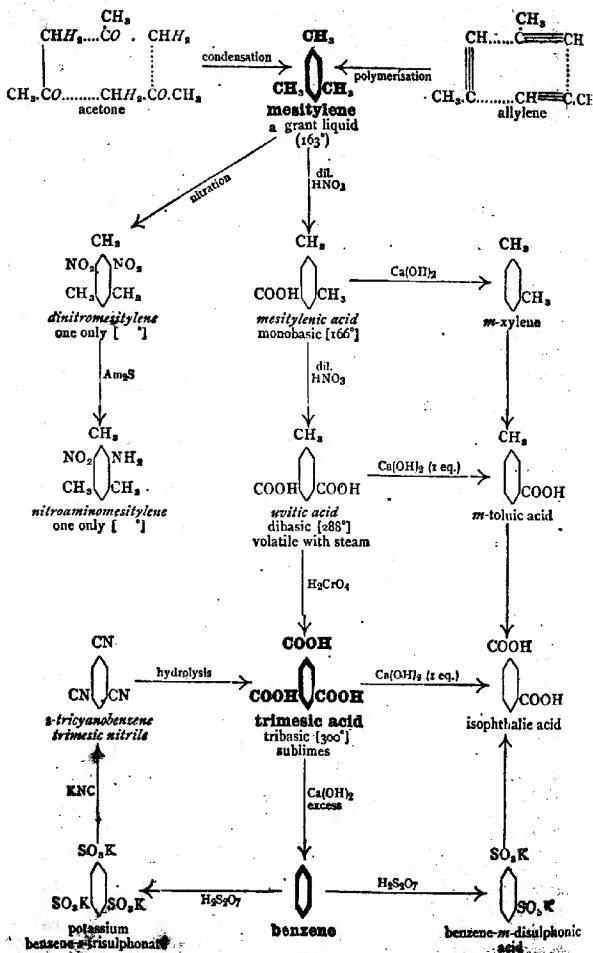


Mellitic acid is also formed by oxidising graphite with alkaline permanganate, and occurs naturally, as *aluminium mellitate*, in honey stone or mellite, a soft mineral which is found embedded in lignite.

As there is no hydrogen in the benzene nucleus, mellithene does not form a sulphonic acid, and is thus insoluble in sulphuric acid; but by prolonged heating with this agent it is degraded to durene and a mixture of the sulphonic acids of the lower methylbenzenes.

**331. Synopsis.**—All the polymethyl-benzenes required by the ring formula are known. Mesitylene, the symmetrical trimethyl-derivative, prepared synthetically from acetone, affords an independent proof of the orientation of meta-xylene and its oxidation products.

## MESITYLENE.



## SECTION XV

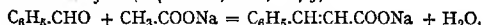
### THE HIGHER ALKYL-BENZENE DERIVATIVES: BRIDGED-RING COMPOUNDS

#### CHAPTER LX

##### THE CINNAMIC GROUP: INDIGO

**332. Cinnamic Acid.**—Besides the immediate derivatives of benzene and the methylbenzenes, there are numerous compounds, which are derived from the higher alkyl benzenes and corresponding olefinic and acetylenic hydrocarbons.

The principal representative of the unsaturated compounds of this class is cinnamic acid. The aldehyde of this acid is the essential constituent of oil of cinnamon, whilst the acid itself occurs naturally in such products as balsam of Tolu, and storax or liquid amber. It is best made synthetically, by condensing benzaldehyde with sodium acetate, in presence of acetic anhydride (Perkin, *sen.*, 1875).



These materials are boiled together in a reflux apparatus for some hours, and after removing the excess of aldehyde (*e.g.* by distillation with steam), and decolorising the hot solution with animal charcoal, the cinnamic acid (which is set free by the acetic acid liberated from the anhydride) is allowed to crystallise; it is recrystallised from water. On a technical scale benzal chloride (§ 275) is substituted for the aldehyde.

Cinnamic acid is also formed by oxidising benzalacetone (§ 276) with dilute sodium hypobromite, the methyl group, as with all methyl ketones (§ 90), being eliminated as bromoform. It may also be made by condensing benzaldehyde with ethyl acetate by means of alcoholic sodium ethoxide (§ 146), the "aldol" which is formed initially being at once dehydrated.

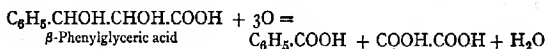
The cinnamic condensation of aromatic aldehydes is of very general applicability. It is a special case of the aldol condensation (§ 146); the aldehyde group condenses with the  $\alpha$ -group of the "acetic" acid (propionic acid yields  *$\alpha$ -methylcinnamic acid*), and, except when the resulting alcoholic group is tertiary, the hydroxy-compound is immediately dehydrated to the olefine. Thus with malonic acid, benzaldehyde forms *benzalmalonic acid*, which yields cinnamic or benzalacetic acid when heated.



**Cinnamic** or *trans*- $\beta$ -phenylacrylic acid,  $C_6H_5.CH:CH.COOH$  (Frémy, 1839), is a crystalline substance which melts at  $133^\circ$  and boils at  $300^\circ$ . Like benzoic acid, it is sparingly soluble in cold water, although freely so in hot water and petroleum.

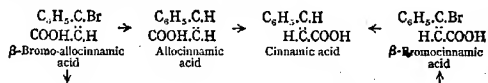
**Ferric cinnamate** is a yellow insoluble powder resembling ferric benzoate. **Ethyl cinnamate**, which is formed in the usual manner, is a fragrant liquid boiling at  $271^\circ$ , and **methyl cinnamate**, a crystalline solid melting at  $33^\circ$  (compare § 123).

Cinnamic acid is a monobasic acid ( $K = 0.0036$ ), and the simple relation to benzene indicated by the syntheses, is confirmed by its conversion into benzaldehyde and benzoic acid when boiled with chromic acid mixture. Its olefinic character is proved by its conversion into a crystalline *dibromide*, and its oxidation by cold alkaline permanganate (§ 104) to the corresponding glycol,  $\beta$ -phenylglyceric acid, which is resolved into benzoic and oxalic acids when further oxidised.



As an unsymmetrical derivative of ethylene, cinnamic acid forms two stereoisomeric modifications. The labile or *cis*-isomeride, *allocinnamic acid*,  $C_6H_5.CH(COOH).CH_3$ , a crystalline substance melting at  $68^\circ$  ( $K = 0.0158$ ), is formed by reducing the corresponding bromo-acid with zinc-dust in alcohol; it is converted into the stable or *trans*-acid by heating, either alone or with concentrated sulphuric acid.

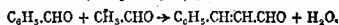
$\beta$ -Bromo-allocinnamic acid, a crystalline compound melting at  $160^\circ$ , which is made by digesting phenylpropionic acid (§ 336) with hydrobromic acid, is similarly converted into  $\beta$ -bromocinnamic acid, which yields ordinary cinnamic acid when reduced.



Cinnamic acid is an  $\alpha:\beta$  unsaturated acid; its additive compound with hydrogen bromide is a  $\beta$ -bromo-acid, and the corresponding hydroxy-acid is consequently unstable, and readily reconverted into the unsaturated acid (§§ 132, 138).  $\alpha:\beta$ -Acids are therefore unaffected by hydrating agents, such as moderately concentrated sulphuric acid, whilst  $\beta:\gamma$ -acids, such as phenylisocrotonic acid (§ 372), are converted into lactones (§ 151). When heated with caustic alkalis, the  $\beta:\gamma$ -acids are converted into the isomeric  $\alpha:\beta$ -acids (Fittig, 1888).

Cinnamic aldehyde may be isolated from oil of cinnamon by shaking with sodium bisulphite; the bisulphite compound is decomposed by sodium carbonate, and the aldehyde separated by distillation with steam.

It is also formed in the normal manner, by distilling calcium cinnamate with calcium formate; and it may be made synthetically in the same way as the acid, by saturating a mixture of benzaldehyde and acetaldehyde with hydrogen chloride (compare § 146).



*Cinnamic aldehyde*,  $C_6H_5.CH:CH.CHO$  (Dumas, 1833), is a very fragrant liquid (compare § 132), which boils unchanged under low pressure; it has the usual properties of an aldehyde, and is readily oxidised and reduced, whilst as an ethylene derivative it forms a crystalline additive *dibromide*.

*Cinnamyl alcohol*,  $C_6H_5.CH:CH.CH_2OH$ , a crystalline substance, of hyacinth odour, melting at  $33^\circ$ , which occurs naturally in storax as a cinnamic ester, is formed by reducing cinnamaldehyde with sodium amalgam; it is a primary aromatic alcohol (§ 280), and an olefinic compound.

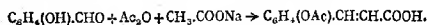
*Coniferyl alcohol*,  $C_6H_5(OH)(OMe).CH:CH.CH_2OH$ , a crystalline phenolic derivative of cinnamyl alcohol, is obtained by hydrolysing the glucoside coniferin (§ 310) with emulsin (§ 171) or dilute acids; when reduced with sodium amalgam, it is converted into eugenol (§ 310).

**333. Substitution Products of Cinnamic Acid.**—As a benzene derivative, cinnamic acid forms many substitution products, some of which are of technical importance.

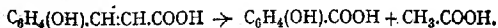
*o-Nitrocinnamic acid*,  $C_6H_4(NO_2).CH:CH.COOH$  (Beilstein, 1872), a crystalline substance melting at  $238^\circ$ , is an intermediate product in the synthesis of indigo (§ 336).

It is formed, with the para-compound, by direct nitration, its *ethyl ester* being separated from the sparingly soluble *p*-ester by fractional crystallisation from alcohol. It is also produced by the action of warm bleaching-powder solution on *o-nitrobenzalacetone*,  $NO_2.C_6H_4.CH:CH.CO.CH_3$ , a crystalline methyl ketone, which is made by condensing *o-nitrobenzaldehyde* with acetone (§ 332).

The hydroxy-acid which is formed by the action of nitrous acid on the corresponding *o*-amino-acid occurs naturally in clover and other plants; it may also be made synthetically. Its *acetyl derivative* is manufactured synthetically from salicylic aldehyde for the sake of the lactone, coumarin, into which it is converted by simply heating.

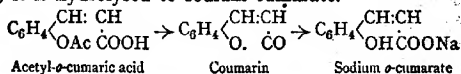


*o-Hydroxycinnamic or orthocumaric acid*,  $C_6H_4(OH).CH:CH.COOH$  (Delalande, 1842), is a crystalline substance melting at  $208^\circ$ ; it is resolved into salicylic and acetic acids when fused with potash.



*Coumarin* or *o-cumaric lactone* (Boullay, 1826), is a crystalline substance melting at  $66^\circ$ ; it occurs naturally in the

common woodruff; it is also present in oil of lavender, and on account of its pleasant odour (that of new-mown hay) is used as the basis of many perfumes. When boiled with alcoholic soda, it is hydrolysed to sodium cumarate.



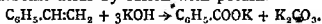
### 334. Phenyl-Ethane, Phenyl-Ethylene, and Phenyl-Acetylene.—

Styrene, the hydrocarbon which is formed by heating cinnamic acid with lime, also occurs free in storax, from which it may be separated by distillation with steam; it can be made synthetically in various ways, and is thus formed, together with benzene, when acetylene is polymerised by heat (compare § 288).

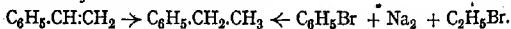


Styrene or *phenylethylene*,  $\text{C}_6\text{H}_5\text{.CH:CH}_2$  (Simon, 1839), is a highly refractive liquid of pleasant odour, boiling at  $144^\circ$ ; it cannot be kept, as it polymerises spontaneously to a glassy substance, *metastyrene*.

As an ethylene derivative styrene absorbs bromine, forming *styrene dibromide*, a crystalline substance melting at  $74^\circ$ ; and it is resolved into benzoic and carbonic acids by fusion with potash.



When styrene is heated in a sealed tube with hydriodic acid or its vapour is passed with hydrogen over hot reduced copper, it is converted into the saturated hydrocarbon phenylethane; \* this compound can also be formed synthetically, and with good yield, from bromobenzene and ethyl bromide by the sodium method.



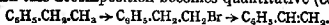
*Phenylethane* or *ethylbenzene*,  $\text{C}_6\text{H}_5\text{.CH}_2\text{.CH}_3$  (Tollens and Fittig, 1864), which is a liquid resembling toluene, boils at  $134^\circ$  and freezes at  $-94^\circ$ . Like its homologue, it yields benzoic acid when boiled with dilute nitric acid, the side chain being disintegrated; this is always the case with such compounds, however long the chain.

When phenylethane is brominated at its boiling point, the halogen enters the side-chain, as in toluene, and phenyl-ethyl bromide is formed.

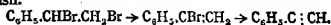
*Phenylethyl bromide* or *ω-bromethylbenzene*,  $\text{C}_6\text{H}_5\text{.CH}_2\text{.CH}_2\text{Br}$ , is a

\* If, however, reduced nickel be substituted for the copper, *ethylcyclohexane*,  $\text{C}_6\text{H}_{11}\text{.C}_2\text{H}_5$ , is formed; it is a light liquid, boiling at  $133^\circ$ .

liquid resembling benzyl bromide; it boils at  $200^{\circ}$ , and at the same time partially decomposes into hydrogen bromide and styrene; with alcoholic potash this decomposition becomes quantitative (compare § 109).



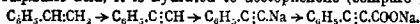
Similarly, on heating styrene dibromide with alcoholic potash, it is converted successively into bromolefinic and acetylenic derivatives. At the boiling point, *bromostyrene*,  $C_6H_5.CBr:CH_2$ , an unstable liquid analogous to vinyl bromide is formed; it may also be prepared by boiling cinnamic acid dibromide with aqueous sodium carbonate. At  $120^{\circ}$ , however, the whole of the bromine is eliminated, and phenyl-acetylene is produced; this is also formed by heating phenylpropionic acid with aniline, and by debrominating *acetophenone bromide*,  $CMePhBr_2$ , with alcoholic potash.



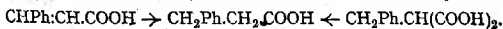
*Phenylacetylene*,  $C_6H_5.C:CH$  (Glaser, 1870), is a colourless liquid, of pleasant, aromatic odour, which boils at  $142^{\circ}$ , and resembles acetylene in its actions.

It forms a white *silver* and a yellow *cuprous compound*, and hot sodium absorbs it, forming a spontaneously inflammable *sodium derivative*, which, like sodium crotonylene, absorbs carbon dioxide, and is converted into the corresponding carboxylate (§ 336).

Phenylacetylene is reduced to phenylethylene when its glacial solution in acetic acid is boiled with zinc, and when treated with moderately concentrated sulphuric acid, it is hydrated to acetophenone (compare § 111).



**335. Hydrocinnamic Acid: Tyrosine.**—On digesting aqueous cinnamic acid with sodium amalgam, it is reduced to phenylpropionic acid, a saturated compound which may also be made from benzyl chloride by the acetoacetic or malonic synthesis.



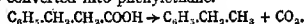
Cinnamic acid

Hydrocinnamic acid

Benzylmalonic acid

*Hydrocinnamic* or  *$\beta$ -phenylpropionic acid*,  $C_6H_5.CH_2.CH_2.CO_2H$  (Erlenmeyer, 1862), is a crystalline substance melting at  $49^{\circ}$ ;  $K = 0.227$  (compare Propionic acid).

It is oxidised to benzoic acid when boiled with chromic acid mixture, the side-chain being disintegrated in the normal manner; when heated with lime it is converted into phenylethane.



The pathological product, tyrosine, which is formed in liver disease, and in the putrefaction and hydrolysis of albumen, is a derivative of this acid; it is prepared by boiling cheese (*trypes*) with potash, or horn with dilute sulphuric acid.

*L-Tyrosine* or *p-hydroxyphenylalanine*,  $C_6H_4(OH).CH_2.CH(NH_2).CO_2H$  (Liebig, 1846), is a crystalline, optically active substance, which melts at  $235^{\circ}$ , and is sparingly soluble in boiling water;  $[\alpha]_D = -8^{\circ}$ .

It has all the characteristics of an amino-acid; forms salts with acids and bases; is converted by nitrous acid into a hydroxy-acid; and is resolved by heat into carbon dioxide and the corresponding amine, *hydroxyphenyl-ethylamine*.

When fused with potash, tyrosine is converted into *p*-hydroxybenzoic acid, acetic acid, and ammonia, and the constitution thus indicated is confirmed by its synthesis from *p*-hydroxybenzaldehyde and hippuric acid.



*p*-Hydroxybenzaldehyde    Benzoylaminoacetic acid    Benzoylamino-hydroxycinnamic acid



On heating these two substances with acetic anhydride and sodium acetate they condense in the "cinnamic" manner, yielding a lactimide or internal aminic anhydride of *p*-hydroxy- $\alpha$ -benzoylamino-cinnamic acid; this lactimide when reduced with sodium amalgam yields inactive benzoyl-tyrosine, from which *i*-tyrosine is obtained by hydrolysis with concentrated hydrochloric acid (Erlenmeyer, jun., 1897.)

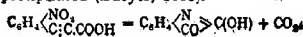
*i*-Benzoyltyrosine is resolvable by the alkaloid method (§ 220) into *d*<sub>1</sub> and *l*-benzoyl-compounds, which yield the optically active *d*- and *l*-tyrosine when hydrolysed; the laevo-compound is identical with the tyrosine from casein.

**336. Phenyl-Propiolic Acid.**—When cinnamic acid dibromide, or better, the dibromide of ethyl cinnamate, is heated with alcoholic potash, it is converted successively into *α*-bromo-cinnamic acid (§ 332), and phenylpropiolic acid.

*Phenylpropiolic acid*,  $\text{C}_6\text{H}_5.\text{C}:\text{C}.\text{COOH}$  (Glaser, 1870), is a crystalline substance, which melts at 136°, and resembles propiolic acid in its actions;  $K = 0.59$ . Its ortho-nitro-derivative, made by digesting the dibromide of onitro-cinnamic acid with cold potash, is convertible into indigo.  $\text{C}_6\text{H}_5.\text{CHBr}.\text{CHBr}.\text{COOH} \rightarrow \text{C}_6\text{H}_5.\text{CH}:\text{CBr}.\text{COOH} \rightarrow \text{C}_6\text{H}_5.\text{C}:\text{C}.\text{COOH}$ .

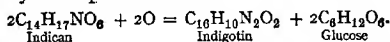
When heated with water at 120°, phenylpropiolic acid is resolved into carbon dioxide and phenylacetylene, from the sodium salt of which it may also be directly synthesised (§ 334). It is reduced to cinnamic acid by zinc and acetic acid, and to hydrocinnamic acid by sodium amalgam; it does not form metallic compounds, because like crotonylene, and unlike propiolic acid, it does not contain "acetylene" hydrogen.

*o*-Nitrophenylpropiolic acid,  $\text{C}_6\text{H}_4(\text{NO}_2).\text{C}:\text{C}.\text{COOH}$  (*o*), is a crystalline substance, which does not melt when heated, but decomposes into carbon dioxide and *o*-nitrophenylacetylene;  $K = 1.06$ . When boiled with aqueous potash, it is converted into isatin, the first oxidation product of indigo, but if a mild reducing agent, such as grape sugar, is also present, indigo itself is precipitated (Baeyer, 1880).



A similar synthesis is effected from *o*-nitrobenzalacetone, indigo being rapidly precipitated when a few drops of caustic soda are added to a solution of *o*-nitrobenzaldehyde in acetone.

**337. Indigo.**—The well-known dye indigo (ινδικόν, the Indian dye) has been used from very early times. It occurs in the various indigofera as a glucoside *indican*, from which it is produced by the hydrolytic action of an accompanying enzyme, followed by atmospheric oxidation.

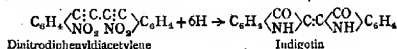


The indigo leaves are macerated with lime and water, and the crude indigo which gradually settles at the bottom of the vat is collected and washed, and finally purified by sublimation; it is formed by the oxidation of indoxyl (§ 338). The essential constituent of indigo is the dye indigo-blue, but related colouring matters such as indigo-red and indigo-purple are also present.

*Indigo blue* or *indigotin*,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{NH} \\ \text{CO} \end{smallmatrix} > \text{C} : \text{C} \begin{smallmatrix} \text{NH} \\ \text{CO} \end{smallmatrix} > \text{C}_6\text{H}_4$ , is a dark blue, insoluble powder, which can be crystallised by sublimation under low pressure, or from boiling aniline or turpentine. Both the vapour and solution are intensely blue, and the crystals and polished powder show a copper-red lustre.

The molecular formula of indigotin follows from its vapour density; its constitution is deduced from its relation to isatin (§ 338), anthranilic acid and aniline, and from a synthesis from phenylacetylene.

The dinitro-derivative of *diphenyldiacetylene*  $\text{C}_6\text{H}_5\text{C} : \text{C} : \text{C} : \text{C}_6\text{H}_5$ , a hydrocarbon which is formed by oxidising *copper phenylacetylene* with alkaline ferricyanide (Baeyer, 1882), yields indigo when digested with ferrous salts in alkaline solution.



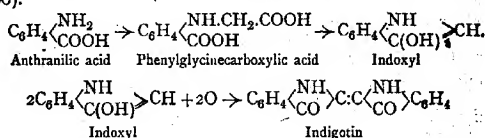
Dinitrodiphenyldiacetylene

Indigotin

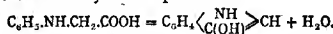
As indigo-blue itself is insoluble in water, it cannot be used directly as a dye, but must first be converted into soluble derivatives, such as can either combine with the fibre, or be precipitated in its substance.

A compound of the first class, *indigo-sulphonic acid*, is formed by dissolving indigo-blue in fuming sulphuric acid; it retains the blue colour of the indigo, and dyes wool directly (Saxony blue). *Indigo-white*,  $\text{C}_{16}\text{H}_{12}\text{N}_2\text{O}_2$ , a colourless substance which is formed by reducing indigo-blue with grape sugar and warm dilute caustic soda, or with alkaline hydrosulphites, is a compound of the second class; the alkaline solution is readily absorbed by the fibre, and on exposing the fabric to air the indigo-white is re-oxidised, and the indigo precipitated (vat dyeing). Synthetic indigo may also be deposited in this manner, as for example by steaming fibre previously printed with alkaline nitrophenyl-propionate.

Indigo is manufactured from anthranilic acid, prepared from naphthalene (§§ 273, 372). Anthranilic acid combines with chloracetic acid, forming *phenylglycine-o-carboxylic acid*,  $\text{COOH.C}_6\text{H}_4\text{.NH.CH}_2\text{.COOH}(o)$ , a crystalline substance which is converted into indoxyl when fused with potash; on oxidising the indoxyl either in acid solution with ferric chloride, or in alkaline solution with air, indigotin is precipitated (Heumann, 1890).



A simple laboratory modification of this process consists in fusing phenylglycine (§ 271) with caustic potash; on exposing the aqueous solution of the orange melt to air, the resulting indoxyl is oxidised to indigo. Indoxyl is also formed by gently warming phenyl-glycine with pyrosulphuric acid; the orange solution is poured on ice, and on adding salt, sodium indigotin-sulphonate (*indigo-carmin*) is precipitated; the indoxyl is here oxidised by the sulphuric acid.



**338. Isatin and Indoxyl.**—When indigo is boiled with dilute nitric or chromic acid, it is converted into isatin, a coloured crystalline substance, which separates on cooling the product; it may also be made synthetically, as from *o*-nitrophenyl-propionic acid (§ 336).

Isatin was first synthesised from *o*-nitrobenzoic acid, the acid chloride of which is converted by the cyanide synthesis into the alkali salt of *o*-aminobenzoylformic or *isatic acid*,  $\text{NH}_2\text{.C}_6\text{H}_4\text{.CO:COOH}$ ; isatin is formed from this by the action of acids (Claisen, 1879).

*Isatin* or *o*-amino-benzoylformic lactame,  $\text{C}_6\text{H}_4\left\langle \begin{array}{c} \text{NH} \\ \text{CO} \end{array} \right\rangle \text{CO}$  (Erdmann, Laurent, 1841), is an orange crystalline substance, which melts at  $201^\circ$ .

In most respects it behaves as a ketone, but it interacts with phosphorus pentachloride in benzene solution in the same way as quinone, forming *isatin chloride*,  $\text{C}_6\text{H}_4\left\langle \begin{array}{c} \text{N} \\ \text{CO} \end{array} \right\rangle \text{CCl}$ , a crystalline substance which melts at  $180^\circ$ , and dissolves to a blue solution in ether.

Isatin is hydrolysed to the *o*-aminobenzoylformate, when boiled with potash, and is immediately re-formed when the acid is set free (compare Lactones, § 151), whence the above

synthesis; on warming its chloride with zinc dust and water, it is converted into indigo.

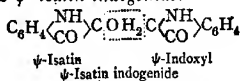
Isatin forms various metallic salts and esters; *O*-ethyl-isatin  $C_6H_4 \begin{smallmatrix} \text{N} \\ \diagup \\ \text{CO} \end{smallmatrix} > C.OEt$ , from the silver salt and ethyl iodide, yields isatic acid when hydrolysed, but the isomeric *N*-ethyl-isatin,  $C_6H_4 \begin{smallmatrix} \text{NET} \\ \diagup \\ \text{CO} \end{smallmatrix} > CO$ , made indirectly through indoxyl, yields *ethyl-anthranilic acid*; isatin itself does not act as an imino-compound, and the *N*-esters are therefore derived from a labile *pseudo-(ψ)-isatin*,  $C_6H_4 \begin{smallmatrix} \text{NH} \\ \diagup \\ \text{CO} \end{smallmatrix} > CO$  (Baeyer, 1883).

When ethyl *o*-nitrophenylpropionate is reduced with ammonium sulphide, it is converted into *ethyl indoxylate*,  $C_6H_4 \begin{smallmatrix} \text{NH} \\ \diagup \\ \text{C(OH)} \end{smallmatrix} > C.COEt$ , a crystalline substance which yields indoxyl when fused with potash; indoxyl may also be obtained directly from indigo by potash fusion, but with soda at 200°, further hydrolysis occurs, and anthranilic acid is formed.

*Indoxyl*,  $C_6H_4 \begin{smallmatrix} \text{NH} \\ \diagup \\ \text{C(OH)} \end{smallmatrix} > CH$ , is an unstable, oily liquid, which is soluble in water, acids and alkalies; the aqueous solution has a yellow fluorescence, and the alkaline solution rapidly absorbs oxygen and precipitates indigo-blue.

Indoxyl condenses with potassium pyrosulphate in warm, aqueous solution, forming *potassium indoxyl sulphate*,  $C_6H_4N.O.SO_2OK$ , which is sometimes present in urine; like indican (§ 337) is slowly oxidised to indigo when exposed to air, and rapidly by ferric chloride in acid solution, and hence is sometimes termed *urine-indican*. Indoxyl, like isatin, forms two classes of alkyl derivatives, the *N*-esters being derived from the unknown labile *ψ-indoxyl*,  $C_6H_4 \begin{smallmatrix} \text{NH} \\ \diagup \\ \text{CO} \end{smallmatrix} > CH_2$ .

Indoxyl readily condenses with aldehydic and ketonic substances, forming indogenides, analogous to the hydrazones; indigotin itself is *ψ-isatin-indogenide*.



*Benzaldehyde indogenide*,  $C_6H_4 \begin{smallmatrix} \text{NH} \\ \diagup \\ \text{CO} \end{smallmatrix} > C:CH.C_6H_5$ , an orange, crystalline substance, melting at 176°, is made by heating benzaldehyde with indoxyl. Similarly, indoxyl condenses with isatin in alkaline alcoholic solution, forming *isatin indogenide*,  $C_6H_4 \begin{smallmatrix} \text{NH} \\ \diagup \\ \text{CO} \end{smallmatrix} > C:C \begin{smallmatrix} \text{NH} \\ \diagup \\ \text{CO} \end{smallmatrix} > C_6H_4$ , a brown; crystalline substance, which is identical with the *indigopurpurin* of commercial indigo; it is also formed together with indigotin when isatin chloride is reduced.



Isatin and indoxyl are oxygenated derivatives of *indole*,  $\text{C}_6\text{H}_4\begin{smallmatrix} \text{NH} \\ \text{CH} \end{smallmatrix} \text{CH}$  (§ 409), a crystalline, feebly basic substance, which may be prepared by distilling indigo with zinc-dust.

**339. Synopsis.**—Cinnamic acid is a phenyl derivative of acrylic acid, and a true unsaturated compound. The pathological product tyrosine is derived from hydrocinnamic acid; the perfume coumarin from *o*-hydroxycinnamic acid; and the dye indigo from the related acetylene derivative, phenylpropionic acid. Corresponding unsaturated hydrocarbons are also known.



## CHAPTER LXI

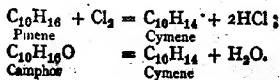
### THE TERPENES: CAMPHANE GROUP

**840. Turpentine and the Pinenes: Cymene.**—Turpentine, the sticky exudation of certain conifers, is a solution of resin (§ 351) in a volatile oil, which is separated by distillation with steam. This spirit or oil of turpentine, which is employed technically as a solvent of oils and resins, is a mixture of isomeric hydrocarbons of neighbouring boiling-point, which are known as the terpenes. The relative amount of these varies with the source of the turpentine; the principal constituent obtained by fractionating the American oil is dextro-pinene, whilst French turpentine yields mainly laevo-pinene.

*d-Pinene*,  $C_{10}H_{16}$  (Berthelot, 1850), is a colourless, insoluble liquid, which boils at  $155^{\circ}$ , and has the characteristic odour of turpentine. It is lighter than water, and dextrogyrate; sp. gr. =  $0.858/15^{\circ}$ ;  $[\alpha]_D = +21^{\circ}$ . *l-Pinene*, its optical antipode, is otherwise identical in properties.

Pinene has the composition of an alkyl-dihydrobenzene (§ 290), and that it is closely related to benzene is shown by its rapid oxidation to *p*-cymene when chlorinated, or heated with iodine or concentrated sulphuric acid. But although convertible into benzenoid compounds, it is not itself benzenoid but olefinic in character; it is essentially an unsaturated, unstable substance, and can rarely be recovered from its derivatives. Its relation to the other terpenes is discussed later (§ 350).

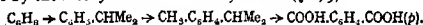
The hydrocarbon cymene, with which most of the terpenes are closely connected, occurs naturally in oil of caraway seed and eucalyptus; it is prepared either by heating oil of turpentine with iodine, or by distilling camphor (§ 341) with phosphorus pentoxide.



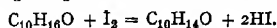
*p*-Cymene or *p*-methyl-isopropylbenzene,  $CH_3.C_6H_4.CH(CH_3)_2$

(*p*), (Gerhardt, 1839), which is a light, insoluble liquid of pleasant odour, boils at  $175^{\circ}$  and freezes at  $-73^{\circ}$ . In its chemical behaviour it resembles the lower alkyl-benzenes, forming *sulphonic acids*, *phenols*, etc.; and that it is a paramethyl-alkylbenzene follows from its oxidation to *p*-toluic and terephthalic acids, when boiled with dilute nitric acid.

The proof of its constitution is completed by direct synthesis. On boiling benzene with isopropyl chloride in presence of aluminium chloride (§ 279), *cumene* or *isopropylbenzene*,  $C_6H_5.CHMe_2$ , is formed, a liquid which resembles cymene and boils at  $153^{\circ}$ ; and on brominating this hydrocarbon, a *bromocumene* is obtained, which is convertible into cymene by the methyl-iodide-sodium synthesis (§ 279).



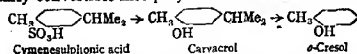
The natural cymene-phenols, carvacrol and thymol, are also closely related to the terpenes; carvacrol, which occurs in oil of garden-cress, and with thymol in oil of thyme, is easily made by boiling camphor (§ 341) with iodine.



*Carvacrol* or 1:4:2-hydroxy-*p*-cymene,  $CH_3 \text{---} \text{C}_6\text{H}_3(\text{OH}) \text{---} CHMe_2$

(Müller, 1869), is a liquid which boils at  $236^{\circ}$ , whilst *thymol*, its 1:4:3-isomeride, is a crystalline solid melting at  $51^{\circ}$ ; both are scarcely soluble in water (compare Polyphenols).

The relation of carvacrol to *p*-cymene is shown by its conversion into this hydrocarbon when heated with phosphorus pentasulphide, and by its synthesis from cymenesulphonic acid by fusion with potash. The ortho-relation of the hydroxyl to the methyl group of carvacrol is demonstrated by its conversion into *o*-cresol when heated with phosphorus pentoxide (the isopropyl being eliminated as propylene). Thymol is similarly convertible into *p*-cymene and *m*-cresol.



When cymene is taken internally, it is excreted as *cuminic* or *cumene-carboxylic acid*,  $CHMe_2.C_6H_4.COOH$ , a crystalline substance, which is also formed by oxidising its aldehyde, *cuminal*,  $CHMe_2.C_6H_4.CHO$ , the essential constituent of oil of caraway.

**341. Camphor and Camphoric Acid.**—The natural product camphor, which is intimately connected with the terpenes and cymene, is extracted from the old wood of the Japanese camphor-laurel by distillation with steam, and is also manufactured artificially from turpentine (§ 344).

*d*-Camphor,  $C_{15}H_{24}O$ , is a transparent, tough, crystalline substance, having a characteristic odour; it melts at  $176^{\circ}$ ,

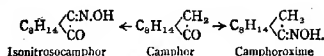
and boils at 209°, but sublimes slowly at ordinary temperatures; its specific rotatory power in alcoholic solution is  $[\alpha]_D = +44^\circ$ . The corresponding *lavo*- and *inactive modifications* differ from it only physically.

The determination of the constitution of camphor and confirmatory synthesis have involved much laborious work, owing to the liability of certain of its derivatives to isomeric change. It is brominated and sulphonated almost as readily as an aromatic compound, but although it is convertible into the benzenoid compounds, cymene and carvacrol, it is a saturated cyclic ketone (§ 287) and not a derivative of benzene.

There are three sets of mono-substitution products, the  $\alpha$ ,  $\beta$  and  $\gamma$  derivatives (§ 342). The  $\alpha$ -halogen compounds are formed by direct substitution of the hydrogen of the  $\text{CH}_2\text{CO}$ -group, whilst the  $\beta$  and  $\gamma$ -compounds are obtained indirectly, usually by decomposing the corresponding sulphonic halides. The  $\alpha$ -chlorobromocamphors and chloronitrocamphors exist in stereoisomeric pairs (compare § 326).

*d*-Camphorsulphonic acid,  $\text{C}_{10}\text{H}_{18}\text{SO}_3\text{H}$ , which is formed by sulphonating camphor in acetic anhydride, is a powerful acid, and forms stable, well-crystallised salts with ammonium and analogous bases. As it is strongly dextrogyrate, its salts with the constituents of racemic ammonium bases (§ 214) are not enantiomorphous, and may be separated by fractional crystallisation.

The ketonic constitution of camphor is demonstrated by its conversion into a *hydrazone* and crystalline *oxime*, and its interconvertibility with a secondary alcohol, *d*-borneol (§ 344); and that the ketonic group is associated with a methylene group is proved by the formation of *benzylidene* and *isonitroso compounds* by condensation with benzaldehyde and nitrous acid (§§ 276, 234).



A saturated ketone of the formula  $\text{C}_{10}\text{H}_{18}\text{O}$  is necessarily a ring compound, for a ten-carbon, open-chain compound of this class would have the formula  $\text{C}_{10}\text{H}_{20}\text{O}$ ; and as the presence of a single carbon ring in the molecule accounts for only two of the missing valencies (§§ 287, 288), at least two rings must be present (compare § 349).

Camphor is therefore a bi-cyclic compound. The ring which contains the ketonic group is ruptured by energetic oxidation; and its nature, with that of the second ring, is determined by a study of camphoric and camphoronic acids, the oxidation products.

When camphor is boiled with concentrated nitric acid, it is oxidised to *d*-camphoric acid, a dibasic acid of which six stereoisomeric forms are

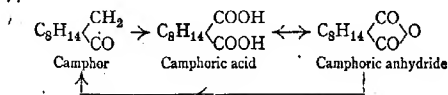
known (§ 342); each of the optically isomeric camphors is connected with a labile or *cis*- and a stable or *trans*-modification (§ 326). The same *d*-acid is formed by the oxidation of  $\alpha$ -bromocamphor or  $\alpha$ -chlorocamphor.

*d*-cis-Camphoric acid,  $C_8H_{14}(COOH)_2$  (Laurent, 1836), is a crystalline substance, which melts at  $187^\circ$ , and has a specific rotatory power  $[\alpha]_D = +50^\circ$ ;  $K = 0.0023$ ; as it forms a *bromo-acid* by direct substitution, and does not at once reduce cold alkaline permanganate, it is a saturated compound.

The hydrocarbon,  $C_8H_{16}$ , from which it is derived, is therefore a cycloparaffin (§ 288), and the acid is analogous in constitution to the dicarboxylic acids of the succinic-adipic series (§ 152).

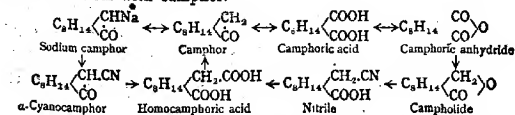
When camphoric acid is distilled, it is resolved into a crystalline *anhydride*, melting at  $221^\circ$ , from which it is recoverable by the usual hydrolysis; and this anhydride may be reconverted into camphor, through homocamphoric acid, the next homologue of camphoric acid (Haller, 1896).

It is therefore clear that the camphor and camphoric acid molecules possess a common nucleus,  $C_8H_{14}C_2$ , and that the bicyclic ketone is converted into the monocyclic acid by a process parallel to the conversion of the monocyclic ketohexamethylene into the open-chain compound, adipic acid (§ 287).



The anhydride is reduced by sodium amalgam to a crystalline lactone, *campholide* (compare § 324), which by heating with potassium cyanide and hydrolysis of the resulting *nitrile*, is converted into the homologous acid. *Homocamphoric acid*,  $C_9H_{16}(COOH)_2$ , which is a saturated dibasic acid, closely resembling its lower homologue, may also be made by hydrolysing  $\alpha$ -cyanocamphor, which is formed by the action of cyanogen bromide on *sodium camphor* (compare § 107).

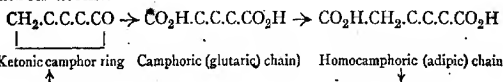
Like barium adipate, barium homocamphorate is resolved by distillation into barium carbonate and the corresponding cyclic ketone (§ 289); and this is identical with camphor.



**342. Constitution of Camphoric Acid and Camphor.**—As adipic acid and its higher homologues do not readily form anhy-

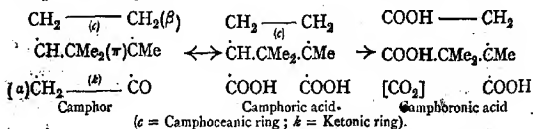
drides (§§ 152, 288), the ready dehydration of camphoric acid (even by digestion with cold acetyl chloride) proves it to be a substituted succinic or glutaric acid. On the other hand, as homocamphoric acid does not form an anhydride, it is at least an adipic acid, as is proved independently by the formation of the cyclic ketone, camphor, when its barium salt is distilled; substituted glutaric acids do not form cyclic ketones directly.

But as homocamphoric acid is not a glutaric derivative, camphoric acid, its next homologue, cannot be derived from succinic acid; it is therefore a substituted glutaric acid; and hence the ketonic ring of the camphor molecule contains five carbon atoms.



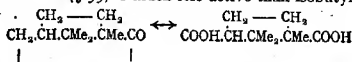
The nature of the second ring remains to be determined. Camphoric acid is resolved by further oxidation into an open-chain, tribasic acid, *camphoronic acid*, a crystalline substance (m.p. 137°), which has been proved synthetically to be  $\alpha\alpha\beta$ -trimethyltricarballic acid,  $\text{COOH.CMe}_2\text{.CMe(COOH).CH}_2\text{.COOH}$ . The cycloparaffin,  $\text{C}_8\text{H}_{16}$ , from which camphoric acid is derived (§ 341), is therefore a trimethyl-compound; hence the non-ketonic ring of camphor also contains five carbon atoms, and is that of a *trimethylcyclopentane*,  $\text{C}_5\text{H}_4\text{Me}_3$ .

This hydrocarbon is known as *camphoceane*, and the corresponding ring in the camphor molecule is termed the *camphoceanic*, as distinguished from the ketonic ring. Camphoric acid is *trimethylcyclopentane-dicarboxylic acid*, and camphor the cyclic ketone of its next higher homologue.



The position of the unchanged (CMe) carboxyl group in the camphoric acid molecule follows from its position in that of camphoronic acid, and the position of the second (CH) carboxyl from the glutaric constitution. This may also be proved independently; camphoric acid forms but one direct bromo-substitution product, *bromocamphoric acid*, which from analogy with saturated aliphatic acids, shows that in its molecule there is but one hydrogenated carbon atom linked to carboxyl.

There is further a great difference in the activity of the two carboxyl groups; *orthoethyl hydrogen camphorate* ( $>\text{CH}.\text{COOEt}$ ), which is formed by the action of sodium ethoxide on camphoric anhydride, is readily hydrolysed, whereas *alloethyl-hydrogen camphorate* ( $>\text{CMe}.\text{COOEt}$ ), which is formed by partial hydrolysis of *diethyl camphorate*, is comparatively resistant to hydrolytic agents. The more active carboxyl, from analogy with aliphatic compounds, is that which is associated with the  $\text{CH}$ -group; trimethyl-acetic acid (§ 99) is much less active than isobutyric acid.

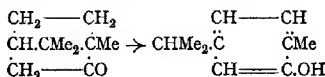


Camphor and Camphoric Acid as Trimethylglutaric Derivatives

As there are two asymmetrical carbon atoms ( $\text{CH}$  and  $\text{CMe}$ ) in the camphoric acid molecule, there are dextro-, laevo- and inactive modifications of the acid, but there is not a second inactive form, as the carboxyl groups are not equivalent. These groups being linked to a saturated carbon ring, each modification further assumes two stereoisomeric forms; in the *cis*-acids the groups are on the same side of the ring, whilst in the *trans*-acids they are on opposite sides (§ 326).

\* The above formulæ render the peculiar double relation of camphor to benzenoid and cycloparaffinoid compounds intelligible. The molecule not only contains the five-carbon camphoceanic ring from which camphoric acid is derived, but also a methylcyclohexane ring, the para-atoms of which are connected by a bridge-group,  $\text{CMe}_2$ .

The bridge is broken by certain reagents, with the result that derivatives of cymene are formed; the bridged-ring is changed into an ordinary benzenoid nucleus.



Camphor

Carvacrol (olefinic formula)

The alternative constitution, in which the  $\text{CMe}_2$ -group is interchanged with a camphoceanic  $\text{CH}_2$ -group, does not account for the formation of *p*-cymene and carvacrol from camphor; the above formulæ were in fact originally constructed by superposing the nucleus of camphoric acid on that of carvacrol (Bredt, 1893). For the same reason the ketonic group is next the  $\text{CMe}$ -group.

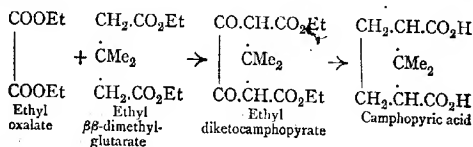
This reasoning is not quite decisive, as it is possible to obtain *m*-cymene and other alkylbenzenes directly from camphor; but it has been fully justified by independent considerations. When, for example, isonitroso-camphor (§ 341) is warmed with hydrochloric acid, it is converted into *α*-camphoramic acid, which is also formed directly by the action of ammonia on camphoric anhydride; the active  $\text{CH}_2$ -group of camphor is here converted into the active carboxyl group of camphoric acid. But this carboxyl is connected with a  $>\text{CH}$ -group (above), so that the active  $\text{CH}_2$ -group of camphor is also linked to this  $>\text{CH}$ -group, and the associated ketonic carbonyl, therefore, to the  $>\text{CMe}$ -group.



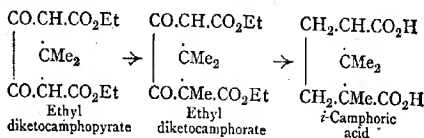


**343. Synthesis of Camphoric Acid and Camphor.**—The constitution of camphoric acid has been finally confirmed by its synthesis from dimethylglutaric and oxalic acids.

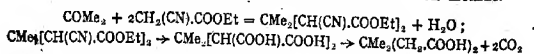
Under the influence of sodium ethoxide (§ 146) the esters of these acids condense to *diketocamphopyric ester*, which is reduced by a somewhat circuitous method to *camphopyric* or *apocamphoric acid* (§ 344), the next lower homologue of camphoric acid.



Ethyl diketocamphopyrate, like ethyl acetoacetate, forms a *sodium compound*, which interacts with methyl iodide forming *ethyl diketocamphorate*, from which, by a similar process of reduction, inactive camphoric acid is obtained (Komppa, 1903).



$\beta\beta$ -Dimethylglutaric acid is made synthetically from acetone and ethylcyanacetate. These substances condense in presence of diethylamine, forming *ethyl  $\alpha\alpha$ -dicyano- $\beta\beta$ -dimethylglutarate*,  $\text{CMe}_2[\text{CH}(\text{CN}).\text{COOEt}]_2$ , a crystalline substance which is converted into the glutaric acid by hydrolysis with moderately concentrated sulphuric acid; the substituted malonic acid, which is formed initially, at once loses carbon dioxide.



**344. The Borneols and Camphenes:** **Camphane.**—Camphor is reduced by sodium in alcohol to two secondary alcohols, borneol and isoborneol, which also occur naturally; they are separable by fractional crystallisation from light petroleum, and are probably stereoisomeric.

*d-Borneol* or *Borneo camphor*,  $C_{10}H_{17}OH$  (Pelouze, 1836) is a crystalline substance which melts at  $204^{\circ}$  and boils at  $212^{\circ}$ ; it sublimes readily, and physically resembles camphor, although more pungent in odour. It is converted by acetic anhydride into a crystalline *acetate*, and is re-oxidised to its ketone, camphor, by dilute nitric acid.

The corresponding *lavo-* and *inactive borneols* are similarly related to *lavo-* and *inactive camphor*.

*Isoborneol*,  $C_{10}H_{17}OH$  (Bertram, 1894), which melts at  $212^{\circ}$ , sublimes with great readiness; its *acetate* is liquid. The acetate is also readily formed by the action of warm acetic acid, in presence of sulphuric acid, on camphene; and together with the latter by heating bornyl chloride (pinene hydrochloride, § 350), with sodium acetate and acetic acid at  $250^{\circ}$ .

Like borneol, isoborneol is reconverted into camphor when oxidised.

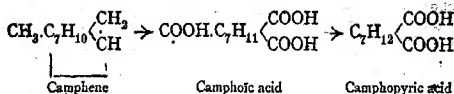
The bornyl halides, which are identical with the pinene hydrohalides (§ 350), are convertible into isobornyl compounds, but the action is not reversible. A similar instability of the acid oxalic ester is utilised in the manufacture of camphor from pinene.



*Bornyl hydrogen oxalate*, which is obtained by heating turpentine with anhydrous oxalic acid at  $130^{\circ}$ , is mixed with alkali and distilled with steam, by which process it is converted partly into *bornyl formate* and carbon dioxide (compare § 128), and partly into camphor and carbon monoxide; the liquid bornyl formate is then oxidised to camphor by heating with chromic acid, and the whole product purified by sublimation in dry steam.

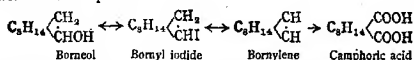
When borneol is dehydrated by phosphorus pentoxide, it is converted into a quasi-saturated, crystalline terpene, camphene, which is a trimethylene derivative; but *bornyl iodide*, which is formed by the action of moist hydrogen iodide on borneol or pinene, is dehalogenised by alcoholic potash mainly to an unsaturated terpene, bornylene.

*d-Camphene* or *isobornylene*,  $C_{10}H_{16}$  (Berthelot, 1858), is a crystalline substance melting at  $152^{\circ}$ , which occurs naturally in various essential oils; it is usually made from pinene (§ 350). When oxidised with nitric acid, it is converted into *camphoic acid*,  $C_8H_{11}(COOH)_3$ , a saturated tribasic acid, which is resolved into the anhydride of *camphopyric acid* (§ 343) when heated (Marsh, 1891).



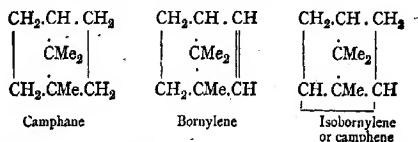
Camphene forms an additive *dibromide*, although with some difficulty, and its hydrochloride is identical with *isobornyl chloride*, which is formed by the action of phosphorus pentachloride on isoborneol, or by the isomerisation of bornyl chloride (pinene hydrochloride); it is therefore obtained when pinene hydrochloride is heated with dilute alkalis. When heated with glacial acetic acid, it is converted into *isobornyl acetate*.

*Bornylene*,  $\text{C}_{10}\text{H}_{16}$  (Wagner, 1900) is a crystalline substance which melts at  $98^\circ$ , and sublimes very readily. When digested with cold alkaline permanganate it is oxidised to camphoric acid (compare § 290), and not to camphoic acid; and it is reconverted into bornyl iodide by moist hydrogen iodide. As it is indifferent to acetic acid, it is readily separable from camphene.



The corresponding saturated hydrocarbon, camphane, is obtained by reducing bornyl iodide with zinc and hydriodic acid, and a compound which is probably identical is formed by reducing camphene with hydrogen in presence of reduced nickel. *Camphane*,  $\text{C}_{10}\text{H}_{18}$  (Aschan, 1900) is a crystalline substance which melts at  $154^\circ$ , and boils at  $162^\circ$ ; it has no action on cold, dilute alkaline permanganate, and is therefore a saturated compound.

Camphane is the mother-substance of the camphor group; borneol and camphor are respectively *hydroxycamphane* and *ketocamphane*. Bornylene is the corresponding olefine, and camphene the isomeric trimethylene derivative (Forster, 1901); the three hydrocarbons constitute a group analogous to propane, propylene and trimethylene.

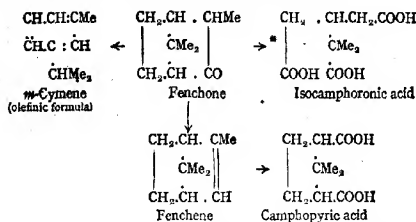


**345. Fenchone and Fenchene.**—Fenchone, a liquid isomeride of camphor, which occurs in oil of fennel (German, *Fenchel*), is of interest by reason of its close resemblance to camphor. *d-Fenchone*,  $\text{C}_{10}\text{H}_{16}\text{O}$  (Wallach, 1890), is a light crystallisable liquid which boils at  $193^\circ$ , and is strongly dextrorotatory,  $[\alpha]_D + 72^\circ$ ; its *lævo*-isomeride, which is found in oil of thuja, is similar.

Fenchone is convertible into *fenchyl alcohol*, *fenchyl chloride* and *fenchene*, by methods practically identical with those used in the conversion of

camphor into borneol, isobornyl chloride and camphene; when oxidised with nitric acid it yields *isocamphoronic acid*,  $\text{COOH.CMe}_2\text{CH}(\text{CH}_2\text{COOH})_2$ , and on distillation with phosphorus pentoxide it is converted into *m*-cymene.

The third methyl group is therefore attached to the ketonic methylene-carbon, which is confirmed by the direct oxidation of the hydrocarbon, fenchene, to camphopyric acid, without the intermediate formation of camphore acid. Fenchone and its derivatives are therefore represented by formulae which differ from those of the camphor group only in the position of the third methyl radical (Gardner, 1898).

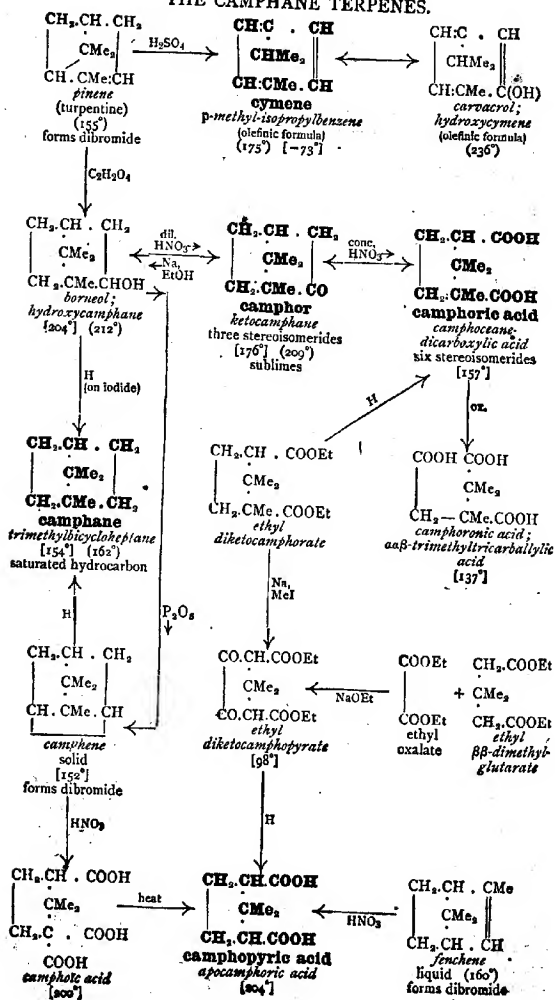


**346. Synopsis.**—The terpenes are unsaturated hydrocarbons, which are closely related to cymene or *p*-methyl-isopropylbenzene.

The camphane terpenes are derived from a saturated, bridged-ring hydrocarbon, camphane or trimethylbicycloheptane, and are distinguished by combining additively with two univalent atoms.

Camphor is ketocamphane, and borneol the corresponding secondary alcohol; camphoric acid, the first oxidation product of camphor, is trimethylcyclopentane-dicarboxylic acid.

## THE CAMPHANE TERPENES.



## CHAPTER LXII

### THE TERPENES: MENTHANE AND OLEFINE GROUPS

**347. The Limonenes: Terpin Hydrate and Terpeneol.**—The chief constituent of the oil of orange and lemon rind is a strongly dextrogyrate terpene, citrene or limonene, which occurs also in other essential oils such as oil of lavender and bergamot.

*d-Limonene*,  $C_{10}H_{16}$  (Schweizer, 1841), is a light, colourless liquid, which boils at  $177^{\circ}$ , and has the characteristic odour of lemons; sp. gr. =  $0.856/15^{\circ}$ ;  $[\alpha]_D = +125^{\circ}$ . *l-Limonene*, its optical antipode, is the principal constituent of the fragrant oil of conifer leaves. *l-Limonene* or *dipentene*, which is obtained by mixing the two isomerides, or by racemisation of either at  $270^{\circ}$ , occurs naturally in oil of cinea, and is also formed by heating pinene or camphene.

Dipentene is thus present in Swedish oil of turpentine, which is isolated by distilling the natural product at a high temperature; it is also formed in a somewhat similar manner by distilling indiarubber, owing to the polymerisation of a simpler hydrocarbon, isoprene or pentadiene (§ 351).

The limonenes differ very markedly from the pinenes and camphenes, and especially from the latter. They are essentially diolefines, and therefore monocyclic compounds (§ 349). Although closely related to cymene (§ 340) and convertible into this hydrocarbon by oxidation with sulphuric acid, they are not benzenoid in constitution, but cyclo-olefinic; they readily form additive products, and break up altogether when oxidised. They are even unstable to hydrolytic agents, and are thus interconvertible with open-chain, aliphatic compounds.

The *limonene tetrabromides*,  $C_{10}H_{16}Br_4$ , are stable crystalline substances; the active modifications,  $[\alpha]_D = \pm 73^{\circ}$ , melt at  $104^{\circ}$ , whilst the inactive modification, formed by melting these together, or from *l-limonene*, melts at  $124^{\circ}$ . The *monohydrochlorides*,  $C_{10}H_{17}Cl$ , which are formed by direct combination with dry hydrogen chloride, are similarly related, but the dihydrochlorides, which result when moisture is present, are identical with one another, and with pinene dihydrochloride (§ 350). *Limonene*

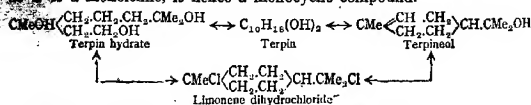
or *dipentene dihydrochloride*,  $C_{10}H_{18}Cl_2$ , is a crystalline substance melting at  $50^\circ$ ; it is reconverted into *i*-limonene when heated with aniline.

The *nitrosochlorides*,  $C_{10}H_{18}NOCl$ , melt at  $103^\circ$ ; the inactive modification is converted by alcoholic potash into *i*-carvoxime,  $C_{10}H_{14}:N.OH$  the oxime of *carvone* or oil of caraway,  $C_{10}H_{14}O$ ; this is a ketonic compound which is readily convertible into the isomeric carvatriol.

Limonene dihydrochloride is hydrolysed by dilute alcohol to a saturated aliphatic alcohol, terpin hydrate, which is also obtained when pinene or limonene is digested with dilute acids. This alcohol is readily reconverted into *i*-limonene, either directly, or through terpin, a saturated cyclic alcohol, and a related unsaturated alcohol, terpineol.

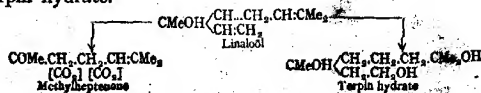
*cis*-Terpin hydrate,  $C_{10}H_{19}(OH)_2$ , is a crystalline substance melting at  $118^\circ$ ; it is reconverted into limonene dihydrochloride by concentrated hydrochloric acid, and into limonene itself by dehydrating agents. When heated alone, terpin hydrate is converted into *cis*-terpin, which by further dehydration, with phosphoric acid, yields terpineol.

*d*-*cis*-Terpineol,  $C_8H_8Me.CMe_2.OH$ , is a crystallisable oil of high boiling-point, which resembles lilac in odour; it may also be made directly from limonene dihydrochloride, and is reconverted into it by concentrated hydrochloric acid. When distilled with potassium pyrosulphate it is converted into *i*-limonene. Terpineol is a tertiary alcohol (§ 98), and as it is a monolefine, is hence a monocyclic compound.



**348. The Olefinic (Open-Chain) Terpenes.**—The constitution of terpin hydrate (and, therefore, in part, of limonene) follows from its formation by the hydration of linalool and geraniol, two open-chain, diolefinic alcohols.

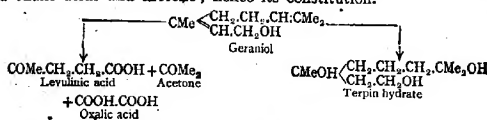
1-*Linalool*,  $CM_2 \cdot CH \cdot CH_2 \cdot CH_2 \cdot CMe(OH) \cdot CH \cdot CH_2$  (Morin, 1881), which occurs naturally in lavender and bergamot, is a fragrant liquid boiling at  $195^\circ$ . When gently oxidised it is converted into *methylheptenone*, a monolefinic ketone whose constitution has been established synthetically; and when shaken with cold, dilute sulphuric acid it is converted into terpin hydrate.



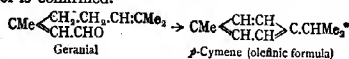
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Linalool is converted by acetic anhydride partly into 4-limonene, and partly into the acetate of the isomeric alcohol, geraniol. *Geraniol* or *lemonol*,  $\text{CMe}_2\text{:CH}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CMe}\text{:CH}\cdot\text{CH}_2\cdot\text{OH}$  (Jacobsen, 1871), a primary diolefinic alcohol, which occurs naturally in roses, lemon-grass and geraniums, is a fragrant, optically inactive liquid; it resembles roses in odour when diluted, and with the corresponding monolefinic alcohol, *rhodinol*,  $\text{CMe}_2\text{:CH}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CHMe}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{OH}$ , forms the essential constituent of attar of roses.

Geraniol, like linalool, is converted into terpin hydrate by cold, dilute sulphuric acid, but is resolved by alkaline permanganate into levulinic and oxalic acids and acetone; hence its constitution.



As a primary alcohol, geraniol forms an aldehyde, *geranial* or *citral*  $\text{C}_9\text{H}_{16}\cdot\text{CHO}$  (which also occurs naturally in oil of lemon-grass), and an acid, *geranic acid*,  $\text{C}_9\text{H}_{16}\cdot\text{COOH}$ . Geranial yields *p*-cymene when distilled with potassium pyrosulphate, whilst geranic acid can be made synthetically from methylheptenone and ethyl iodacetate by the magnesium method (§ 98): in both cases the constitution deduced from the oxidation of the alcohol is confirmed.



When geraniol itself is dehydrated, it does not form a cyclic compound but an open-chain, triolefinic terpene. *Geraniene*,  $\text{CMe}_2\text{:CH}\cdot\text{CH}_2\cdot\text{CH}\cdot\text{CMe}\text{:CH}\cdot\text{CH}_2$ , is a light, terpenoid liquid boiling at  $174^\circ$ ; it rapidly resinifies by absorption of oxygen, and as a triolefine forms a crystalline *hexabromide*. *Myrcene*, a similar unstable terpene occurring in oil of bay, is also converted into *terpin hydrate* by dilute sulphuric acid.

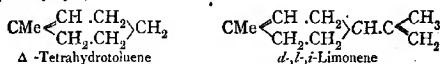
The easy resolution of these terpenoid compounds into comparatively simple aliphatic products, renders it not improbable that they may be formed naturally, with the related terpenes, by progressive condensation, and that terpenoid molecules may be built up automatically in a very similar manner to those of the natural sugars,—from such materials as formaldehyde, acetone, acetic acid, and carbohydrate derivatives of the type of levulinic acid.

**349. Constitution and Synthesis of Limonene: Menthol and Menthane.**—As limonene forms a tetrabromide, it is a diolefiné, and therefore a monocyclic compound, and not a bicyclic or bridged-ring compound like camphor and the camphenes (§ 341)\*. Its convertibility into carvacrol suggests a six-carbon ring containing para-methyl and isopropyl groups, and this inference is supported by its interconvertibility with

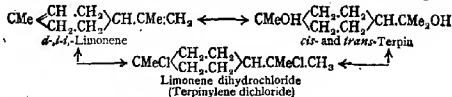


terpin hydrate and terpineol. The entire absence of *p*-toluic and terephthalic acids, and cycloid acids of the camphoric type from the products of its oxidation render it unlikely, however, that the isopropyl group is present as such; hence it follows that one of the olefinic linkages is situated in the "isopropyl" side-chain.

The limonenes are thus tetrahydrotoluenes, containing a  $\beta$ -propenyl group in the para-position (Wagner, 1894). Their characteristic odour appears to be dependent on the concurrent presence of double linkages in the ring and side-chain (compare § 290).

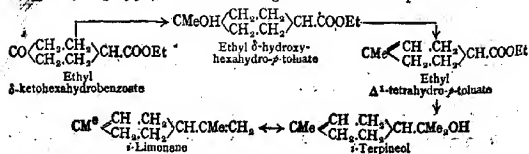


The  $\Delta^1$ -position of the cycloid olefinic linkage (§ 326), which is established by the relation of the hydrocarbon to terpineol and geranial, renders the molecule asymmetrical (C) and capable of optical activity; in the dihydrochloride, however, this asymmetry disappears, and hence the same inactive product is obtained from all three limonenes. For the same reason terpineol can assume optically active forms, whilst terpin can only form stereoisomerides of the hexahydroterephthalic type (§ 326).



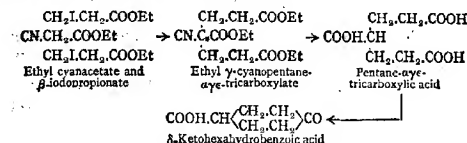
The constitution of the compounds of the limonene group has been verified by the synthesis of inactive terpineol from ethyl  $\delta$ -ketohexahydrobenzoate by the magnesium methiodide method (§ 98); the terpineol thus obtained is interconvertible with *i*-limonene (§ 347), which is identical with the natural product (Perkin, jun., 1904).

The *p*-keto-group of the ketonic acid is first converted into a CMeOH-group, by treatment with magnesium methiodide; the hydroxyhexahydrotoluic ester, thus formed, is then dehydrated; finally the carbethoxy group of the resulting tetrahydrotoluic ester is similarly converted into a CMe<sub>2</sub>OH-group (§ 98), thus converting the ester into terpineol.

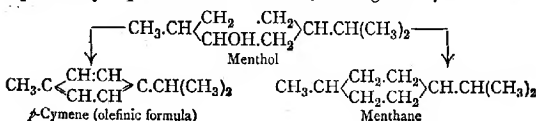


Ketohexahydrobenzoic acid is made synthetically from ethyl cyanacetate and ethyl  $\beta$ -iodopropionate, two molecules of the latter being linked

to the methylene carbon of the former by the sodium method (§ 148a). The cyano-tricarboxylate thus obtained is converted by the usual hydrolysis into a substituted malonic acid, which at once loses carbon dioxide, yielding *pentane-αγγ-tricarboxylic acid*,  $\text{COOH}.\text{CH}(\text{CH}_2.\text{CH}_2.\text{COOH})_2$ . This tricarboxylic acid is converted into the keto-acid when boiled with acetic anhydride and distilled.



The saturated cycloparaffin, hexahydrocymene, which is the mother-substance of the limonene group of compounds, is formed by reducing *menthyl iodide*, an ester of menthol or peppermint camphor. *Menthol*,  $\text{C}_{10}\text{H}_{19}.\text{OH}$ , is a crystalline substance, melting at  $142^\circ$ , which is readily dehydrated to cymene. *Menthane* or *terpane*,  $\text{CH}_3.\text{C}_6\text{H}_{10}.\text{CHMe}_2(p)$ , is a liquid of cycloparaffinoid character, boiling at  $167^\circ$ .



The terpenes of the monocyclic or limonene group are termed *hydroaromatic terpenes*, or terpenes of the *terpane* or *menthane* group. The menthane terpenes are diolefines, and form tetrabromides, whilst the camphane and open-chain terpenes are respectively monolefines and triolefines, and form dibromides and hexabromides.

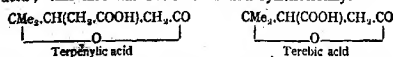
Metaterpenes and orthoterpenes are also known, and some of them have been made synthetically (Perkin, jun., 1905). *Sylvestrene*, from Swedish turpentine, is a derivative of *metacymene*, precisely analogous to limonene in constitution.

**350. Constitution of the Pinenes.**—The pinenes occupy a position intermediate to the camphane and menthane terpenes; they are unstable, unsaturated substances, and although convertible into most of their isomerides, they cannot be recovered from them. They are characterised by forming with nitrosyl chloride at a low temperature a stable, crystalline *nitrosochloride*,  $\text{C}_{10}\text{H}_{16}:\text{NOCl}$  (Tilden, 1875); from which inactive pinene may be recovered in a pure state.

*Terpenylic acid*,  $C_7H_{11}O_2 \cdot COOH$ , melts at  $57^\circ$ , and has been proved synthetically to be the lactone of  $\beta$ -hydroxyisopropyl-glutaric acid; it yields terebic acid when oxidised with permanganate. *Terebic acid*,  $C_8H_9O_2 \cdot COOH$ , which melts at  $174^\circ$ , is hydrolysed by baryta at  $170^\circ$  to

350] *The Terpenes : Menthane and Olefine Groups* 469

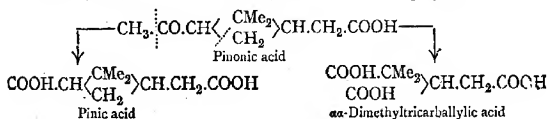
acetone and succinic acid, whence it is the lactone of hydroxyisopropylsuccinic acid; this also has been confirmed synthetically.



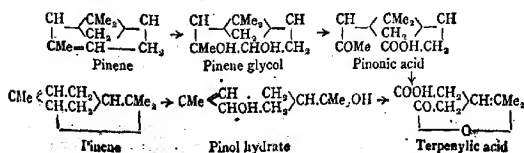
$\alpha$ -Pinonic acid,  $\text{CH}_3\text{CO}\cdot\text{C}_7\text{H}_{12}\cdot\text{COOH}$ , which melts at  $104^\circ$ , and boils unchanged at  $117^\circ$ , is a ketonic monobasic acid, and is oxidised by sodium hypobromite in the manner characteristic of methyl ketones (§ 90), to bromoform and pinic acid; a similar oxidation is effected by dilute nitric acid, when terpenylic acid is also formed. When boiled with alkaline permanganate,  $\alpha$ -pinonic acid is converted into isocamphoronic acid (§ 345). Pinic acid,  $\text{C}_7\text{H}_{12}(\text{COOH})_2$ , which melts at  $102^\circ$ , is a saturated dibasic acid; it is a very stable compound, and resists further oxidation.

Pinol hydrate or *sobrerol*,  $\text{C}_{10}\text{H}_{16}(\text{OH})_2$ , which is a hydroxy-terpineol (§ 347), melts at  $131^\circ$ ; when heated with dilute sulphuric acid, it is dehydrated to the corresponding internal ether, *pinol*,  $\text{C}_{10}\text{H}_{16}\text{O}$ , which is a liquid boiling at  $184^\circ$ . Pinol glycol,  $\text{C}_{10}\text{H}_{16}\text{O}(\text{OH})_2$ , which is formed from pinol by the action of cold, dilute alkaline permanganate (§§ 104, 290), melts at  $129^\circ$ , and is oxidised to terpenylic acid by the same agent at a higher temperature.

As pinic and pinonic acids are saturated compounds, and derived from a hydrocarbon,  $\text{C}_7\text{H}_{14}$ , they are necessarily cycloid in constitution; and the conversion of the ketonic acid into dimethyltricarballic acid indicates that the nucleus of this cycloparaffin is dimethylcyclobutane,  $\text{C}_4\text{H}_6\text{Me}_2$ .

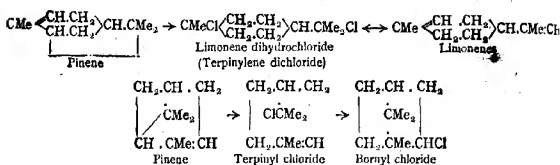


The pinene molecule therefore contains a dimethylcyclobutane nucleus, as well as the reduced benzene ring indicated by its close relation to cymene and carvacrol (Wagner, 1894). In the oxidation to pinonic acid this nucleus, which is known as the picean ring (*Pinus picea*), remains intact, whilst the tetrahydrobenzene ring is broken at the olefine linkage; but in the oxidation to terpenylic acid the picean ring is severed before the benzene ring is attacked.



Pinene is thus a bridged-ring terpene, in which the  $\text{CMe}_2$ -bridge of the camphane terpenes (§ 344) is linked to a meta-CH-group of the reduced benzene ring, instead of to a para- $\text{CMe}$ -group. Its convertibility into bornyl chloride and cymene, as well as into *i*-limonene, is accounted for by the intermediate formation of monocyclic terpineol derivatives (§ 349) by the breaking of the bridge; once broken, this apparently can only be reconnected in the para-position, and hence the transformations of pinene are irreversible:

The relation of pinene to limonene is somewhat analogous to that of camphene to bornylene, the conversion into limonene dihydrochloride being effected by the breaking of the picean ring.



**351. The Polyterpenes and Hemiterpenes: Resins.**—*Caoutchouc*,  $(\text{C}_8\text{H}_8)_x$ , the solidified milky sap of the indiarubber plant, is polymeric with and closely related to the terpenes; it cannot be crystallised, but is precipitated by alcohol in white curds from its chloroform solution. Its molecular weight is unknown, but from its colloid nature is undoubtedly very high.

Caoutchouc combines readily with sulphur, forming vulcanised indiarubber, vulcanite, etc.; these are elastic substances of all degrees of hardness, which retain their elasticity over very wide ranges of temperature.

When indiarubber is distilled, it is converted into a hemiterpene. *Isoprene*,  $\text{CH}_2 \cdot \text{CMe} \cdot \text{CH} \cdot \text{CH}_2$ , which is identical with the synthetic open-chain diolefine, *methyl-butadiene* (Ipatieff, 1897), is a mobile liquid boiling at  $35^\circ$ ; it is unstable, and when kept gradually polymerises to dipentene and caoutchouc.

In addition to this hemiterpene and complex polyterpene, *sesquiterpenes*,  $\text{C}_{15}\text{H}_{24}$ , are known, such as occur naturally in hop oil, etc., as well as *diterpenes*,  $\text{C}_{20}\text{H}_{32}$ .

The residue, which remains in the still after the distillation of turpentine with steam, solidifies to the well-known glassy resin, colophony; this consists mainly of a complex acid derived from phenanthrene (§ 378).

Common resin dissolves almost entirely in caustic alkalies, and on neutralising the clear solution with hydrochloric acid is reprecipitated in

white curds, from which this acid, abietic acid, is extracted by boiling alcohol. The same acid is obtained by distilling colophony under diminished pressure, or with superheated steam.

*Abietic* or *dekahydrotetracarboxylic acid*,  $C_{18}H_{27}COOH$ , is a crystalline substance which melts at  $146^{\circ}$ . It yields resorcinol, protocatechuic acid, etc., when fused with potash, and it is closely related to the terpenes, as it yields isophthalic and terebic acids on oxidation.

When the acid is heated, it is decomposed in the normal manner into carbon dioxide and *abietene* or *methyl-isopropyl-dekahydrophenanthrene*,  $CH_3.C_{14}H_{18}.CHMe_2$  (§ 378).

As an acid, melted resin dissolves metallic oxides, and hence is used in soldering. The solution of resin in caustic soda is used in paper making for rendering the fibres ink-proof; the alkaline solution having been mixed with the pulp, and thus diffused into the substance of the fibre, the insoluble resin acid is precipitated within it by addition of alum.

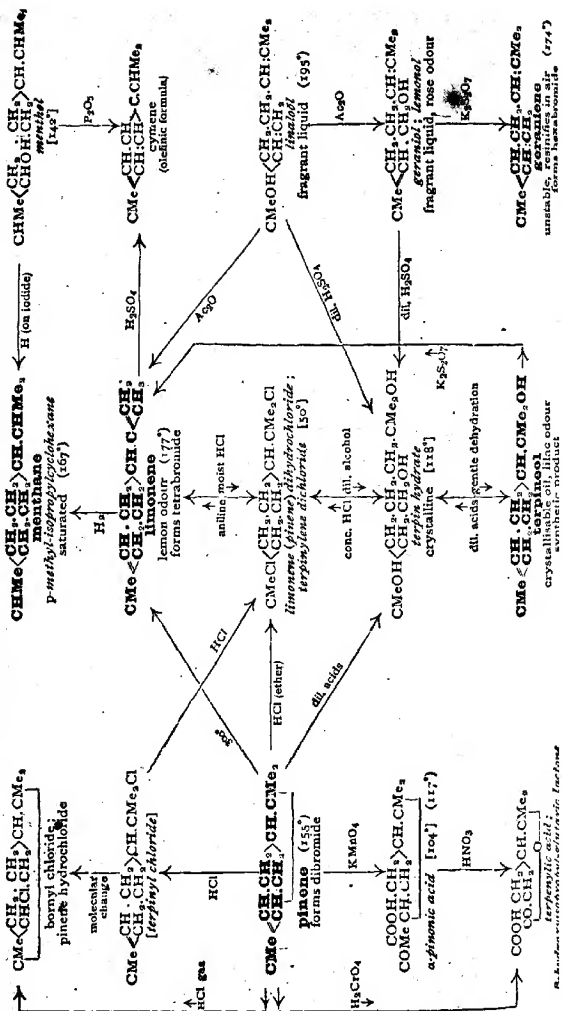
The ordinary varnishes are simply solutions of various resins—colophony, copal, mastic, etc.—in turpentine or other solvents, and the natural balsams, such as Canada balsam, are similar more or less viscid solutions. Amber is a fossil resin, which yields resin acids and volatile terpenes when distilled, as well as succinic acid. The lacs are similar substances.

**352. Synopsis.**—The menthane terpenes are derived from a saturated monocyclic hydrocarbon, menthane or *p*-methyl-isopropylcyclohexane, and are characterised by combining with four univalent atoms; like the camphane terpenes, they are closely related to cymene, but they are also interconvertible with open-chain, aliphatic compounds.

The pinenes are monolefinic bridged-ring terpenes, which are convertible into terpenes of the menthane and camphane groups, but cannot be recovered from them.

The open-chain terpenes are triolefines, and are characterised by combining with six univalent atoms.

## THE MENTHANE AND OPEN-CHAIN TERPENES.



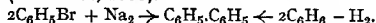
## SECTION XVI

### MULTIPLE-RING COMPOUNDS

#### CHAPTER LXIII

##### DIPHENYL, DIPHENYLMETHANE, AND DIPHENYLETHANE

**353. Diphenyl: Benzidine.**—Benzenoid radicals not only combine with alkyl radicals, but with one another, and when bromobenzene is boiled with sodium in toluene it is thus converted into diphenyl or phenylbenzene (compare § 279); this hydrocarbon is formed in a similar manner by heating benzene vapour to redness, and is conveniently prepared in this way (Berthelot, 1866).



Benzene is dropped slowly into a long, inclined iron tube, which is filled with pumice and maintained at a dull red heat; the product is collected in a heated receiver to eliminate unchanged benzene, and then fractionated and recrystallised from alcohol. Diphenyl is similarly formed from mercury diphenyl (§ 256); it may also be made by eliminating the amino-groups (§ 260) from its diamino-derivative, benzidine; and by the action of reduced copper on benzenediazonium sulphate in acetic anhydride.

*Diphenyl* or *phenylbenzene*,  $\text{C}_6\text{H}_5\cdot\text{C}_6\text{H}_5$  (Fittig, 1862), is a colourless, crystalline substance, which melts at  $71^\circ$ , and boils at  $254^\circ$ . The constitution indicated by its mode of formation is confirmed by its oxidation to benzoic acid, when boiled with chromic anhydride in glacial acetic acid.

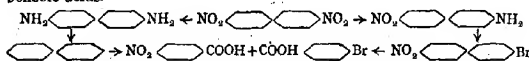
*Ditolyl* and other analogous compounds are known.

As the diphenyl molecule contains two benzene rings, the isomerism of its substitution products is complicated; each substituted group may be in the ortho-, meta, or para-position relatively to the second phenyl radical. *pp-Dinitrodiphenyl*,  $\text{NO}_2\cdot\text{C}_6\text{H}_4\cdot\text{C}_6\text{H}_4\cdot\text{NO}_2$  (*p, p*), a crystalline substance melting at  $233^\circ$ , which is formed, together with the *op*-derivative, by direct nitration, is of interest from its connection with benzidine, the base of the cotton azo-dyes (§ 384).



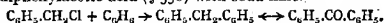
*Benzidine* or *pp-diaminodiphenyl*,  $\text{NH}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{C}_6\text{H}_4 \cdot \text{NH}_2$  (Zinin, 1845), a crystalline basic substance which melts at  $122^\circ$ , is manufactured from azobenzene derivatives (§ 380).

Its constitution is proved by its formation by reduction of the nitro-compound, and by its conversion into diphenyl when the amino-groups are eliminated by the diazonium method; the orientation of the amino-groups is established by the conversion of the dinitro-compound through the nitro-amino and nitro-bromo-compounds into *p*-nitro- and *p*-bromo-benzoic acids.



**354. Diphenylmethane.**—When benzyl chloride interacts with benzene under the influence of aluminium chloride or aluminium amalgam, a radical is introduced into the benzene ring in the normal manner, and benzyl-benzene is formed.

The same hydrocarbon is produced by heating benzophenone in a sealed tube with hydriodic acid and red phosphorus, and can be extracted from the cold product with ether. It is also formed by heating benzene with methylal (*i.e.* formaldehyde) and concentrated sulphuric acid; and by distilling diphenylacetic acid (§ 356) with soda-lime.



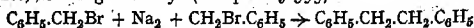
*Diphenylmethane* or *benzylbenzene*,  $\text{C}_6\text{H}_5 \cdot \text{CH}_2 \cdot \text{C}_6\text{H}_5$  (Jena, 1870), is a crystalline substance which melts at  $27^\circ$ , and boils at  $261^\circ$ ; it resembles oranges in odour. Like diphenyl, it forms nitro- and other substitution-products; but on oxidation with chromic acid mixture it is reconverted into its ketone, in which respect also it differs from aliphatic hydrocarbons.

The corresponding secondary alcohol, which is formed by reducing benzophenone with sodium amalgam, is also obtained by heating *diphenylmethyl bromide*,  $\text{C}_6\text{H}_5 \cdot \text{CHBr} \cdot \text{C}_6\text{H}_5$ , in a sealed tube with water.

When diphenylmethane vapour is passed through a red-hot tube, it is converted into *fluorene* or *diphenylmethylene*,  $\text{C}_6\text{H}_4 \cdot \text{CH}_2 \cdot \text{C}_6\text{H}_4$ , a crystal-

line, fluorescent substance melting at  $113^\circ$ ; the action is analogous to the conversion of benzene into diphenyl.

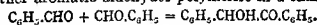
**355. Dibenzyl: Benzoin.**—When a benzene solution of benzyl chloride is boiled with sodium, the benzyl radicals unite, forming dibenzyl (compare § 353).



\* *Dibenzyl* or *s-diphenylethane*,  $\text{C}_6\text{H}_5 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{C}_6\text{H}_5$  (Cannizzaro, 1862), which is a crystalline substance melting at  $52^\circ$ , is the mother substance of a group of paraffinoid alcohols and ketones, the most prominent of which are benzoin and benzil.

### 356] *Diphenyl, Diphenylmethane, Diphenylethane* 475

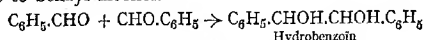
The alcohol-ketone, benzoin, which is polymeric with benzaldehyde, is formed by heating a dilute alcoholic solution of the latter with potassium cyanide at 100°, the intermediate cyanhydrin condensing with unchanged aldehyde. Other aromatic aldehydes polymerise in a similar manner.



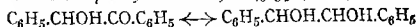
*Benzoin*,  $C_6H_5 \cdot CHOH \cdot CO \cdot C_6H_5$  (Liebig and Wöhler, 1830), is a crystalline substance melting at 137°; it is reduced to dibenzyl by hydriodic acid at 250°, and oxidised by concentrated nitric acid to the corresponding diketone, benzil. As a ketone, it forms condensation products with hydroxylamine and phenylhydrazine.



When benzoin is reduced with sodium amalgam in cold alcoholic solution, it is converted into the corresponding glycol, hydrobenzoin, which is also formed, by a pinacone condensation (§ 92) during the reduction of benzaldehyde to benzyl alcohol.



*Hydrobenzoin* or *s-diphenylglycol*,  $C_6H_5 \cdot CHOH \cdot CHOH \cdot C_6H_5$ , is a crystalline substance which melts at 139°, and boils at a high temperature; it is reoxidised to benzoin (and benzil) by nitric acid, but is reconverted into benzaldehyde by chromic acid mixture; when boiled with dilute sulphuric acid it is converted into *diphenylacetaldehyde* (§ 356).



As the hydrobenzoin molecule contains two asymmetrical carbon atoms, it assumes four stereoisomeric forms. Ordinary hydrobenzoin is optically inactive and irresolvable, and therefore an internally compensated or meso-compound (§ 163).

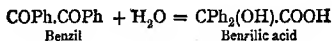
If, however, benzaldehyde is reduced while boiled with water, mainly the racemic modification is formed; this is more conveniently obtained from its *acetate*, which is prepared by boiling stilbene dibromide (§ 357) with potassium acetate and glacial acetic acid.

*Isobenzoin*,  $C_6H_5 \cdot CHOH \cdot CHOH \cdot C_6H_5$ , which is a crystalline substance melting at 121°, is optically inactive, but may be resolved into *dextro*- and *levo*-modifications by the ordinary methods; in its general actions it is practically identical with the meso-compound.

**356. Benzil: Stereoisomerism of Oximes.**—The diketone, which is obtained when benzoin is heated gently with concentrated nitric acid, separates as a yellow oil, which solidifies when poured into water.

*Benzil* or *diphenylglyoxal*,  $C_6H_5 \cdot CO \cdot CO \cdot C_6H_5$  (Laurent, 1834), is a pale yellow, crystalline substance, melting at 95°; it is

soluble in cold alcoholic potash to a violet solution, from which it is precipitated unchanged by acids; if, however, the solution is boiled, the colour disappears and benzoic acid is formed (compare Pinacolin, § 92).



*Benzilic* or *diphenylglycollic acid*,  $\text{C}_6\text{H}_5.\text{C}(\text{OH})(\text{COOH}).\text{C}_6\text{H}_5$  (Liebig 1837), which is best obtained by heating benzoin with aqueous soda, in a stream of air, is a crystalline substance melting at  $148^\circ$ ; when heated with hydriodic acid it is reduced to *diphenylacetic acid*,  $\text{CHPh}_2.\text{COOH}$  which yields diphenylmethane (§ 354) when distilled with lime.



Analogous compounds are obtained similarly from substituted benzaldehydes. Anisaldehyde (§ 309) gives *p-anisoin*, *anisil*, and *anisilic acid*; and cuminal (§ 340) gives *p-cuminoin*, *cuminil* and *cuminilic acid*.

There are two monoximes and three dioximes of benzil, the isomerism of which is probably analogous to that of maleic and fumaric acids (Hantzsch, 1892).



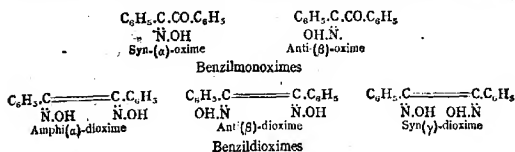
A study of the configuration of the cyanogen radical leads to the conclusion that the valencies of a tervalent nitrogen atom are not in one plane, or they could not correspond with the three valencies of the triply-linked cyanogen carbon; if, therefore, the doubly-linked nitrogen atom of an oxime be pictured at the apex of a tetrahedron, so that its valencies proceed towards the angles, the third valency may lie in either of two directions, corresponding with the *cis*- and *trans*-positions of malcoid and fumaroid compounds (§ 155).

If the oximino-group is capable of interaction with one of the groups attached to the doubly-linked carbon-atom, it can only so interact when it is in the near or *syn*-position; in the *anti*-position it is too remote. Hence synaldoximes are dehydrated to nitriles by acetyl chloride, whilst antaldoximes form acetates (§ 276); similarly *synphenyl tolyl ketoxime* is converted into *o-toluidic anilide* by the Beckmann transformation (§ 272), whereas the stereoisomeric *anti-oxime* yields *benzorthotoluidide*.

$\alpha$ -*Benziloxime*, which is formed at low temperatures, and melts at  $138^\circ$ , is converted by prolonged heating, especially in presence of alcohol, into  $\beta$ -*benziloxime*, which melts at  $114^\circ$ ; both forms are hydrolysed normally by hydrochloric acid

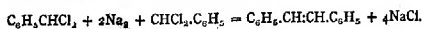
# 358]. *Diphenyl, Diphenylmethane, Diphenylethane* 477

*Benzil-α-dioxime*, which is the most stable of the three dioximes, is formed in the ordinary manner; it melts at 237°. *Benzil-γ-dioxime*, which is made by the action of hydroxylamine on the β-monoxime, melts at 166°, but is then transformed into the β-dioxime. *Benzil-β-dioxime*, which melts at 207°, is converted in alcoholic solution at 180° into the α-dioxime



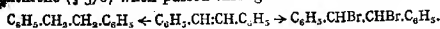
**357. Stilbene and Tolane.**—The ethylene derivative corresponding with dibenzyl is obtained by distilling benzyl sulphide and other benzyl compounds.

It may also be prepared by dechlorinating benzal chloride with sodium, and by a cinnamic condensation from benzaldehyde and phenylacetic acid, carbon dioxide being eliminated.



*Stilbene* or *s-diphenylethylene*,  $\text{C}_6\text{H}_5\cdot\text{CH}:\text{CH}\cdot\text{C}_6\text{H}_5$  (Laurent, 1844), forms large, colourless, brilliant crystals (*σταλβαρ*), melting at 124°; as an olefinic compound it forms an additive *dibromide*, a crystalline substance melting at 237°.

It is reduced by hydriodic acid to the corresponding ethane derivative, dibenzyl, and is oxidised to benzoic acid by chromic acid mixture, and to phenanthrene (§ 378) when passed through a red-hot tube.



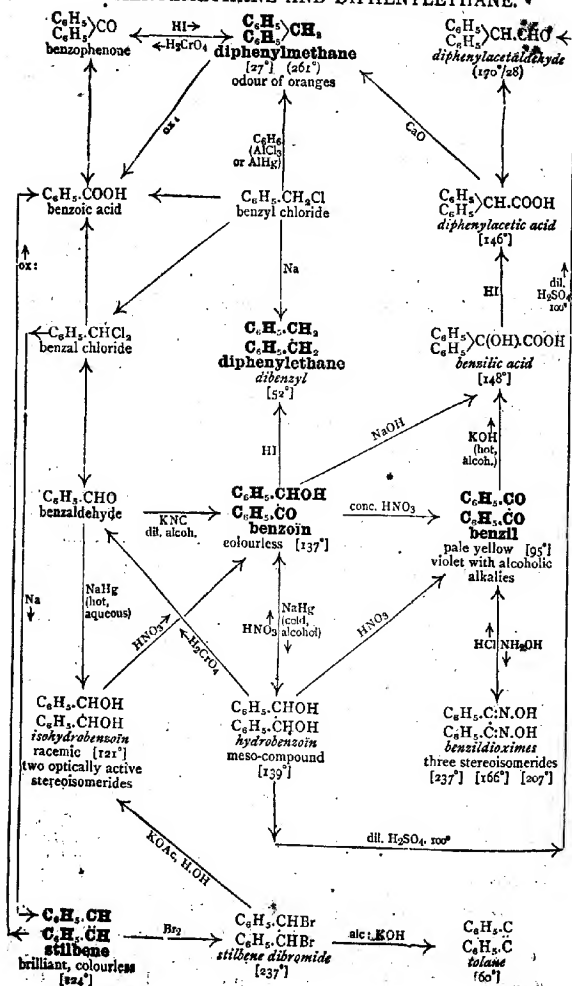
Stilbene dibromide is converted into hydrobenzoin acetate when heated with metallic acetates, and it also loses all its bromine when heated with alcoholic potash, being converted into the corresponding acetylene derivative, tolane.



*Tolane* or *diphenylacetylene*,  $\text{C}_6\text{H}_5\cdot\text{C}:\text{C}\cdot\text{C}_6\text{H}_5$  (Limpricht, 1868), is a crystalline substance melting at 60°; as an acetylene derivative, it forms an additive dibromide and tetrabromide.

**358. Synopsis.**—The phenyl and benzyl radicals combine with each other in the same way as alkyl radicals, forming hydrocarbons containing two benzene rings. Dibenzyl or diphenylethane is connected with a set of alcohols, ketones and unsaturated hydrocarbons, in the same way as an aliphatic hydrocarbon.

## DIPHENYLMETHANE AND DIPHENYLETHANE.



## CHAPTER LXIV

### THE TRIPHENYLMETHANE GROUP: THE ROSANILINES

**359. The Rosanillines.**—The well-known dye magenta is a derivative of a complex hydrocarbon, triphenylmethane. With the exception of a few compounds such as picric acid and murexide, the dye-stuffs used prior to the middle of the nineteenth century—indigo, madder, cochineal, etc.—were of natural origin; they are now to a large extent supplanted by the artificial “aniline” dyes.

Mauve, the first such dye made (Perkin, 1856), is a complex substance, which is formed by oxidising crude aniline sulphate with potassium dichromate, and magenta is synthesised similarly by heating crude aniline with arsenic acid (Medlock, 1860) or mercuric chloride (technically, with nitrobenzene in presence of ferric chloride).

Pure aniline does not yield the dye, nor do the ortho- and para-toluidine with which it is associated in the commercial base, but a mixture of the three amines in molecular proportions gives even better results than the crude material. In the same way, a mixture of aniline and *p*-toluidine yields pararosaniline chloride, a base homologous with magenta. The corresponding acetates, sulphates, etc., are also used as dyes.

In the manufacture of magenta, the hydrochloric acid solution of the mixed amines is heated at  $190^{\circ}$  with the requisite amount of nitrobenzene, and small quantities of iron filings are added periodically. After several hours' heating, the unchanged aniline, etc., is distilled off with steam, and the rosaniline hydrochloride is extracted with boiling water, and precipitated from the solution with salt. The ferrous chloride, which is formed initially, acts as a carrier, being alternately oxidised by the nitrobenzene, and reduced by the mixed amines (compare § 371).

*Rosaniline chloride, magenta, or fuchsine*,  $C_{20}H_{20}N_3Cl$  (Verquin, 1860), is an almost black crystalline substance, having a green pseudo-metallic lustre; it is freely soluble in water and alcohol to an intensely crimson solution, which dyes silk and wool a fast purple-red. *Pararosaniline chloride*,  $C_{18}H_{18}N_3Cl$  (Rosenstiehl, 1876), from aniline and *p*-toluidine differs from

magenta only in that its colour is of a less bluish shade; both compounds are feebly basic, and although themselves ammonium salts (§ 361) combine unstably with acids.

**360. Dyes and Mordants.**—Both rosaniline and pararosaniline salts dye silk and wool a purple-red, and the colour is fast, that is to say, is not washed out by soap and water. But on treating cotton fabrics in this manner, the dye, although of much the same hue and depth, is no longer fixed, and can be washed out of the material. Similarly, picric acid dyes silk, wool, and cotton a bright yellow, but only the silk and wool colours are fast.

As we have noted in the case of indigo (§ 337), the permanence of a dye is due to one or other of two factors: either it is itself precipitated in the body of the fibre, or it combines with some constituent of the latter, forming an insoluble or indiffusible compound. In both silk and wool there are constituents of the nature of amino-acids (§ 224), with which acid dyes like picric acid, and basic dyes like the rosanilines probably form such compounds; and these fibres are therefore coloured permanently by dyes of this class.

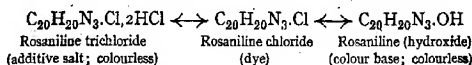
The cellulose of cotton, however, is practically a neutral substance, and only in rare cases (§ 384) combines with colouring matters. In order to dye cotton, therefore, a mordant must be introduced into the fibre, that is to say, a substance which forms an insoluble compound with the dye.

With picric acid, for example, the calico, etc., is soaked in a solution of alum, and then in dilute ammonia, by which the alum, diffused through the substance of the fibre, is converted into insoluble alumina. On now immersing the fabric in the dye-bath, the acid combines with this base, forming a yellow insoluble compound, which cannot be washed away.

The colour produced in this manner is of course that of the mordanted compound, and is often different from that of the dye itself (§ 376). To dye cotton with basic dyes such as the rosanilines, an acid mordant is requisite, and for this purpose tannin or a metallic tannate is usually employed; with some dyes silk and wool have themselves to be mordanted.

**361. Constitution of the Rosanilines: Triphenylmethane.**—The molecule of rosaniline chloride contains three nitrogen atoms, all of which are aminoid, and potentially basic; as already indicated, the dye itself, although an "ammonium" salt, is still feebly basic, and combines additively and unstably with concentrated hydrochloric acid; and the corresponding hydroxide, which is set free from it by caustic alkalis (compare § 362), has marked, although transient, basic properties.

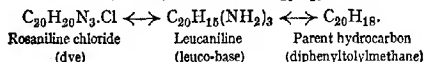
This dihydrochloride, and the free hydroxide or colour base, are both colourless, but easily revert to the dye.



*Rosaniline trichloride*,  $\text{C}_{20}\text{H}_{20}\text{N}_3\text{Cl}_2 \cdot 2\text{HCl}$ , is a colourless, unstable substance, which is reconverted into the coloured monochloride by excess of water. *Rosaniline*,  $\text{C}_{20}\text{H}_{20}\text{N}_3\text{O}$ , the colour base, is a colourless, crystalline substance, which is unstable even in air, and is reconverted into the coloured ammonium salt by dilute acids.

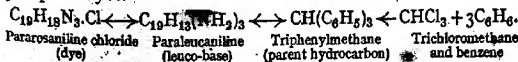
When rosaniline chloride is reduced with zinc dust and hydrochloric acid, it undergoes a more permanent bleaching, analogous to the conversion of indigo into indigo-white (§ 337). The disappearance of the colour is here due to the formation of a leuco-base, *leucaniline*, which can be set free with caustic soda, and extracted with ether.

*Leucaniline*,  $\text{C}_{20}\text{H}_{21}\text{N}_3$  (Hofmann, 1862), is a colourless, crystalline substance, melting at  $100^\circ$ . Unlike free rosaniline, it is stable in air, but it is reconverted into the dye by mild oxidising agents; it is markedly basic, although less so than the colour base, and its actions show that it is the triamino-derivative of a complex hydrocarbon,  $\text{C}_{20}\text{H}_{18}$  (below).



As a primary triamine, leucaniline forms a stable, crystalline *trihydrochloride*, and is converted by nitrous acid into a *trihydroxy-compound*,  $\text{C}_{20}\text{H}_{18}(\text{OH})_3$  (compare Aurin, § 362). When it is warmed with sodium nitrite in acid alcoholic solution, the three amino-groups are eliminated (§ 260), and the triamine is converted into the parent hydrocarbon (E. and O. Fischer, 1878).

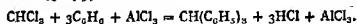
Pararosaniline chloride, the next homologue of rosaniline chloride, behaves throughout in a similar manner, yielding a colour-base, leuco-base and hydrocarbon, homologous with those obtained from rosaniline. This hydrocarbon is triphenylmethane; it may also be made synthetically, and can readily be reconverted into the dye (§ 362). Triphenylmethane is therefore the mother-substance of the rosaniline group of dyes.



The synthesis of the hydrocarbon, which also affords the best method



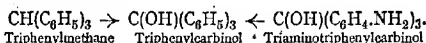
of preparing it, is effected from chloroform and benzene by the aluminium chloride method (§ 279).



The anhydrous, freshly prepared chloride is added to the dry mixture of benzene and chloroform, and after the action has ceased the product is poured into water, and the heavy insoluble layer is fractionated; the fractions distilling below  $300^\circ$  contain diphenylmethane, etc., but the higher fractions solidify on cooling, and after crystallisation from benzene, and drying at  $100^\circ$  to drive off benzene of crystallisation, are recrystallised from alcohol.

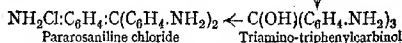
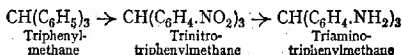
*Triphenylmethane*,  $\text{CH}(\text{C}_6\text{H}_5)_3$  (Kekulé, 1872), is a colourless crystalline substance, which melts at  $92^\circ$ , boils at  $359^\circ$  and has an odour of citron; its constitution is obvious from its mode of formation.

When oxidised with chromic anhydride in acetic acid solution, triphenylmethane is converted into the corresponding tertiary alcohol, *triphenylcarbinol*,  $\text{CPh}_3\text{OH}$ , a crystalline substance melting at  $159^\circ$ ; and as this alcohol is also formed by eliminating the amino-groups from pararosanine by the diazonium method, it follows that the colour-base is its triamino-derivative.

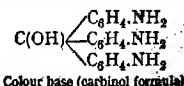
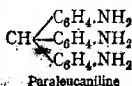


Rosaniline is proved similarly to be the corresponding derivative of *diphenyltolylmethane* (E. and O. Fischer, 1878).

**362. Synthesis of Pararosanine from Triphenylmethane: Quinonoid Structure.**—The above results are confirmed by the preparation of pararosanine from synthetic triphenylmethane, through its trinitro-compound (Fischer, 1879).



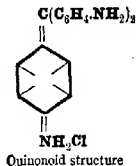
Hence the leuco-base, *paraleucanine*, is *p-triaminotriphenylmethane*, and the related colour base, *pararosanine*, is *p-triaminotriphenylcarbinol* (or the isomeric ammonium hydroxide, below); *leucanine* and *rosanine* being the corresponding derivatives of *diphenyltolylmethane*.



When triphenylmethane is dissolved in fuming nitric acid, and the product is poured into water, a crystalline *trinitro-derivative*,  $C_{19}H_{13}(NO_2)_3$ , is obtained, which on reduction with zinc dust in glacial acetic acid solution, is converted into the corresponding *triamino-compound*,  $C_{19}H_{13}(NH_2)_3$ ; this can be precipitated from the diluted product with ammonia.

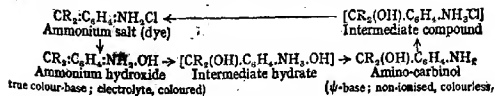
On heating the dry triamino-triphenylmethane on platinum foil with some concentrated sulphuric acid, it is oxidised to the corresponding *carbinol*, and this, when acidified with dilute hydrochloric acid, yields a dye which is identical with pararosaniline chloride; the same dye may also be obtained directly by adding chloranil (§ 304) to the hot alcoholic solution of the triamine.

The constitution of the dyes themselves at one time gave rise to much controversy, but it is now generally agreed that they are quinonoid compounds. All the para-quinones, including those of naphthalene (§ 373) and anthracene (§ 375), are highly coloured substances, and it has been found possible to arrange the formulæ of practically all coloured organic compounds on the quinonoid model (Armstrong, 1888; compare also § 381).



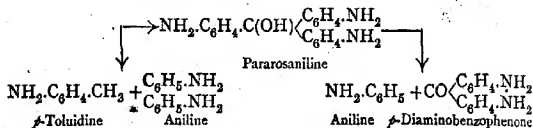
According to the quinonoid formula, the rosaniline dyes are quaternary ammonium salts, from which it follows that the alkaline compounds, which are liberated from them transiently by a single equivalent of alkali, are quaternary ammonium hydroxides. This conclusion is not really inconsistent with the synthetical data, which show the colour-base itself to be a carbinol, for in the absence of acid ions the nitrogen of the ammonium base becomes tervalent; the highly ionised, alkaline solution thus becomes non-ionised, and the unstable, soluble ammonium base is transformed into the neutral, insoluble carbinol.

The carbinol is thus a pseudo-base, comparable with the pseudo-acids (§ 259); although neutral and non-basic, it combines with a single equivalent of acid, re-forming a quinonoid ammonium salt, in which the nitrogen is once more quinquevalent (Hantzsch, 1900).

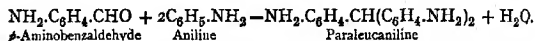


Pararosaniline is hydrolysed to aniline and p-diaminobenzo-

*phenone* (§§ 272, 367) by prolonged heating with hydrochloric acid, but it is reconverted into aniline and *p*-toluidine by hydriodic acid at 200°.



Its leuco-base is probably formed synthetically, in the same way as that of malachite green (§ 366), namely by condensation of the aniline with *p*-aminobenzaldehyde, which may well occur transiently during the oxidation of the toluidine.

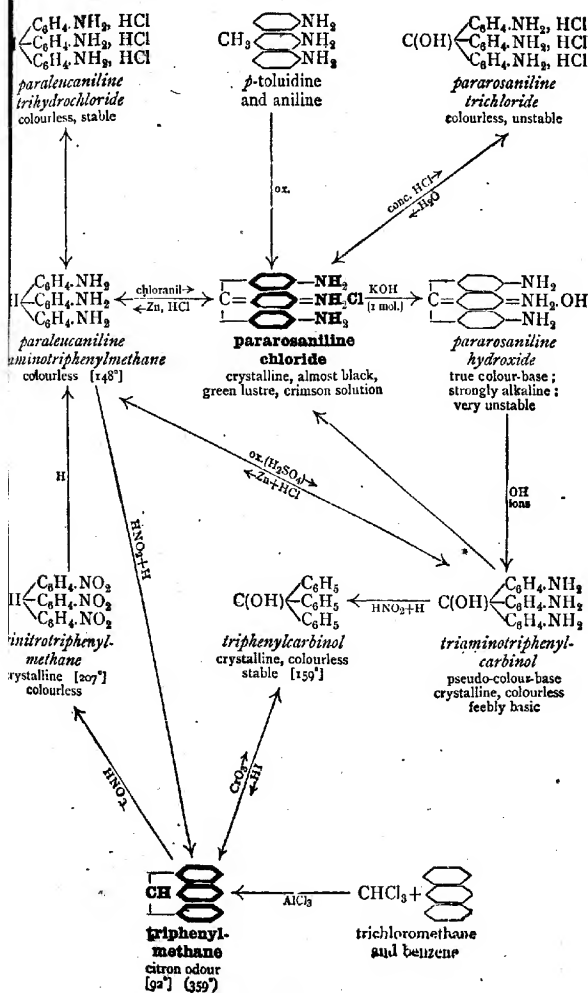


The phenolic or hydroxy-compounds, aurin and rosolic acid, which correspond with the rosanilines, and are formed from them by the diazonium interaction, are made by heating phenol or a mixture of phenols with oxalic or arsenic acid and concentrated sulphuric acid.

*Aurin*,  $\text{O:C}_6\text{H}_4\text{:C(C}_6\text{H}_4\text{OH)}_2$  (Kolbe, 1861), is a dark red crystalline substance, which like the rosanilines has a metallic lustre; it dissolves freely in alcohol and alkalis—in the latter to dark red solutions, but is of no use as a dye, as it cannot be satisfactorily fixed. Aurin is reconverted into pararosaniline by ammonia, and rosolic acid is similarly converted into rosaniline itself.

**363. Synopsis.**—Rosaniline and pararosaniline are quinonoid ammonium salts, derived from triphenylmethane and its next homologue; leucaniline and paraleucaniline, their colourless reduction products, being the corresponding triamino-derivatives; the free ammonium hydroxides are unstable and rapidly change to colourless derivatives of triphenylcarbinol.

# CONSTITUTION OF PARAROSANILINE.



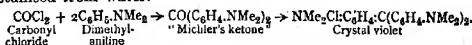
## CHAPTER LXV

### THE TRIPHENYLMETHANE GROUP: ROSANILINE DERIVATIVES AND PHTHALEINS

**364. The Alkyl Rosanilines.**—When alkyl and phenyl radicals are introduced into the amino-groups of rosaniline, the colour gradually changes through violet to blue, and by further addition of methyl chloride or iodide to these derived dyes, green double ammonium salts are produced.

A mixture of such violet methyl-pararosanilines is obtained by heating pararosaniline chloride with methyl chloride; these are usually made, however, from the methyl-anilines, the hexamethyl-compound, which is an intensely violet, basic dye, being prepared from dimethylaniline.

On leading carbonyl chloride into a mixture of this base with aluminium chloride, a crystalline substance, *tetramethyl-p-diaminobenzophenone*, is formed, by an action analogous to that involved in the preparation of benzophenone itself from benzoyl chloride and benzene (Michler, 1876); and on heating this ketonic substance for some hours at 100° with phosphorus oxychloride and a further quantity of the dimethylaniline, it condenses to the colour-base of hexamethyl-pararosaniline. The product is repeatedly extracted with boiling dilute hydrochloric acid, and the chloride thus formed is precipitated from the solution with salt, and re-crystallised from water.



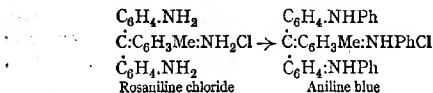
*Hexamethyl-pararosaniline chloride* or *crystal violet*,  $\text{NMe}_2\text{Cl}\cdot\text{C}_6\text{H}_4\cdot\text{C}(\text{C}_6\text{H}_4\text{NMe}_2)_2$  (Hofmann, 1873), is a greenish-black crystalline substance, which, like most of the aniline dyes, has a marked metallic lustre; it dissolves in water and alcohol to a deep violet solution, and dyes silk, wool, and cotton (mordanted with tannin) the same colour.

When heated with methyl iodide, crystal violet is converted into the corresponding methiodide, *iodine green*,  $\text{NMe}_2\text{Cl}\cdot\text{C}_6\text{H}_4\cdot\text{C}(\text{C}_6\text{H}_4\text{NMe}_2)_2\cdot\text{CH}_3\text{I}$ .

The pure hexamethyl dye is not much used in practice, as *methyl violet*, a similar and much less expensive mixture of hexa- and lower methyl-pararosanilines, can be obtained by directly oxidising dimethylaniline. This base is simply warmed with potassium chlorate and copper sulphate for some hours; the dissolved copper is then removed with sulphuretted hydrogen, and the dye is extracted from the product with hot water, and precipitated with salt.

The corresponding methochloride, *methyl green*, is made by passing methyl chloride vapour into a warm alcoholic solution of methyl violet. Methyl nitrate and methyl sulphate have also been used for this purpose, but are objectionable on account of the explosive character of the first, and the poisonous nature of the second.

**365. The Phenyl Rosanilines.**—Whilst the introduction of alkyl groups into the rosanilines gives all shades of violet, pure blues are obtained by introducing phenyl groups.



Triphenyl-rosaniline or aniline blue is thus obtained by heating rosaniline acetate with aniline for several hours at  $180^\circ$ ; the product is extracted with dilute hydrochloric acid, and the chloride precipitated with the concentrated acid.

*Aniline blue* or *triphenylrosaniline chloride*,  $\text{NHPhCl}:\text{C}_6\text{H}_3\text{Me}:\text{C}(\text{C}_6\text{H}_4\cdot\text{NHPh})_2$  (Girard, 1862), is an almost black substance, which is freely soluble in alcohol to a dark blue solution, and dyes silk and wool a pure blue. The dye itself is insoluble in water, but is readily converted into a soluble sulphonie acid (compare § 337). Aniline blue yields diphenylamine when distilled, and the corresponding pararosaniline derivative can be made by heating diphenylamine (§ 250) with oxalic acid, the latter supplying the nuclear carbon.

The sodium sulphonate, *water blue*, is only faintly coloured, whilst the acid itself is as intensely blue as the original dye; the fabric (mordanted with tannin in the case of cotton) is therefore passed through a bath of dilute acid after dyeing.

In this connection the important basic dye, methylene blue, may be mentioned, as it is a derivative of diphenylamine, although not of triphenylmethane.

Methylene blue is made by passing sulphuretted hydrogen into a solution of *p*-amino-dimethylaniline (§ 296), in presence of ferric chloride. The product assumes an intensely blue colour, and the double chloride of the dye with zinc is precipitated by adding zinc chloride and common salt to the aqueous extract. The formation of the blue colour in the above manner affords a very delicate test for sulphides.

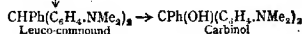
*Methylene blue*,  $\text{NMe}_2\text{Cl} \cdot \text{C}_6\text{H}_3\langle\text{N}\rangle\text{C}_6\text{H}_3\text{NMe}_2$  (Caro, 1876),

is freely soluble in water, and dyes cotton (mordanted with antimony tannate) a fine indigo blue, which is fast to light, and to alkalis and acids.

**366. Malachite Green: Colour of Aniline Dyes.**—The important green dye, malachite or benzaldehyde green, is related to the rosanilines; it is a methylated diamino-triphenylmethane, and is manufactured from benzaldehyde (or benzo-trichloride) and dimethylaniline.

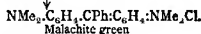
The mixed liquids are heated with anhydrous zinc chloride on a water-bath for some hours, and after removing unchanged dimethylaniline by distillation with steam, the resulting *leuco-compound* is dissolved in dilute hydrochloric acid, and oxidised to the *carbinol* by means of freshly precipitated lead peroxide; the dissolved lead is precipitated with sodium sulphate, and the carbinol converted into the *double zinc chloride* of the dye by precipitation with zinc chloride.

$\text{CHPh}:\text{O} + 2\text{C}_6\text{H}_5\text{NMe}_2$   
Benzaldehyde Dimethylaniline



Leuco-compound

Carbinol



Malachite green

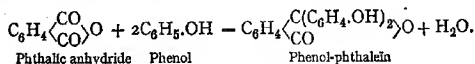
*Malachite green* or *tetramethyldiaminotriphenylmethane chloride*,  $\text{NMe}_2\text{C}_6\text{H}_4\text{CPh}(\text{C}_6\text{H}_4\text{NMe}_2)_2\text{Cl}$  (O. Fischer, 1877), is an almost black, crystalline substance, which dissolves in water to a dark green solution; it is a basic dye, and dyes silk, wool, and cotton (mordanted with tannin) a dark green, which is both less costly and faster than methyl green.

The *colour base*, which is precipitated from the solution by excess of caustic alkali, is a colourless crystalline substance, like the corresponding rosaniline compound; as a pseudo-base or carbinol; however, it is considerably more stable than free rosaniline, and is only slowly converted into the dye on acidifying its solution at ordinary temperatures (compare § 362).

Triphenylmethane, although not itself coloured in the usual sense of the word, thus forms an extensive series of derivatives in which its hydrogen is replaced by salt-forming groups, such as amidogen; it is therefore termed a *chromogen* (Witt, 1876). The selective absorption of light which renders a substance coloured is in most organic compounds conditioned by the quinonoid structure of the molecule (§ 362), whilst the character and extent of the absorption, that is to say, the actual colour, is largely dependent on the nature of the substituent groups (see also § 381).

The "malachite" dye formed from *p*-nitrobenzaldehyde gives practically the same shade as malachite green itself, so that the nitro-group has little or no influence on the colour, whereas the reduction of the nitro to an amino-group changes the green to a reddish-violet. Methylation of this amino-group converts the reddish-violet dye into the purer colour of crystal violet, whilst finally the addition of methyl chloride or iodide to this reconverts the violet into green (iodine green).

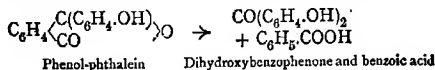
**367. The Phthaleins.**—The last group of triphenylmethane derivatives we have to consider comprises a number of coloured and other compounds, which are formed by condensing the various phenols with phthalic anhydride. The well-known alkali indicator, phenol-phthalein, is thus obtained by heating excess of phenol with phthalic anhydride (§ 324) and concentrated sulphuric acid.



The heating is continued for several hours, after which the product is boiled with water, to remove phthalic and sulphuric acids, and distilled with steam to remove the excess of phenol; the phthalein is then extracted from the insoluble portion with dilute caustic soda, and precipitated from the crimson solution with acetic acid.

*Phenol-phthalein*,  $\text{C}_6\text{H}_4\begin{smallmatrix} \text{C}(\text{C}_6\text{H}_4\text{OH})_2 \\ \diagup \diagdown \\ \text{CO} \end{smallmatrix} \text{O}$  (Baeyer, 1876), is a sandy, crystalline substance melting at 250°; it is freely soluble in alcohol to a colourless or yellowish solution, but is insoluble in water. It dissolves in alkalies to a deep crimson solution, the colour of which is discharged by all acids, even carbonic acid, and by many acid salts; it is therefore useful as an alkali indicator (as with feeble organic acids), but it is useless as a dye, as the colour cannot be fixed.

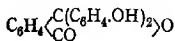
When phenol-phthalein is fused with potash it is converted into benzoic acid and *dihydroxybenzophenone*, the decomposition being analogous to that of pararosaniline into aniline and diaminobenzophenone by hydrochloric acid (§ 362).



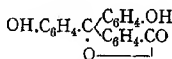
The relation to triphenylmethane thus suggested is traced through *phthalophenone* or *diphenylphthalide*, a crystalline substance which is formed synthetically from phthalyl chloride and benzene by the aluminium chloride method; this is convertible into both phenolphthalein and triphenylmethane.



Phenol-phthalein is thus a derivative both of phthalic acid and of triphenylmethane; it is *dihydroxy-diphenylphthalide*, and the *lactone* of *dihydroxy-triphenylcarbinol-carboxylic acid*.



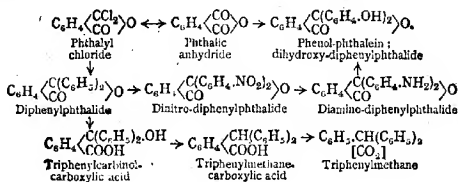
Phenol-phthalein  
as hydroxy-diphenylphthalide.



Phenol-phthalein  
as lactone of carbinol acid.

Diphenylphthalide is converted into the *dinitro-phthalide* by direct nitration, and this is reduced to the diamino-phthalide in the usual manner; the dihydroxy-compound obtained from this by the nitrous acid interaction is identical with phenol-phthalein, which is therefore *dihydroxy-diphenylphthalide*.

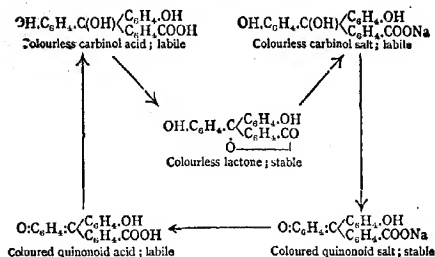
When, on the other hand, diphenylphthalide is boiled with concentrated alcoholic potash, it is hydrolysed to *potassium triphenylcarbinol-carboxylate*, which is reduced by zinc dust and alkali to *triphenylmethane-carboxylic acid*; on distilling the latter with lime, triphenylmethane is obtained; diphenylphthalide or phthalophenone is therefore the *lactone* of *triphenylcarbinol-carboxylic acid*, and phenol-phthalein the corresponding dihydroxy-compound.



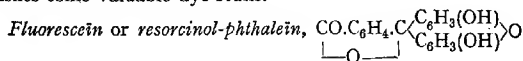
The striking change of colour produced by dissolving phenolphthalein in alkali is again due to the conversion of the phthalein into a quinonoid compound; the alkali salt yields a bright yellow, crystalline *oxime*.

The alkali carbinol-carboxylate obtained by dissolving phenol-phthalein in a large excess of alkali, is colourless, as is the acid which is liberated by exactly neutralising this salt. This carbinol acid is unstable, and is rapidly dehydrated to the lactone in hot solution; but the sodium salt cannot form a lactone, and, except in presence of a large excess of alkali, is at once dehydrated to the salt of a labile quinonoid acid.

Hence when phenol-phthalein is dissolved in a single equivalent of alkali, the crimson colour of the quinonoid salt is at once developed, but on acidifying the alkaline solution, the colour as rapidly disappears, the feeble quinonoid acid reverting to the more stable lactonic condition; for a similar reason, the crimson alkaline solution is also decolorised by a large excess of alkali, owing to the conversion of the coloured quinonoid salt into the colourless carbinol-carboxylate.



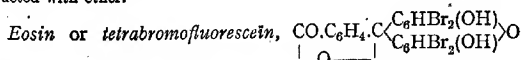
Although phenol-phthaleïn and the homologous compounds made from cresols, etc., are useless as dyes, the analogous resorcinol derivative, which is made in the same way, furnishes some valuable dye-stuffs.



(Baeyer, 1876), is a dark red, crystalline substance, which is insoluble in water, but soluble in alcohol and alkalis; the alkali solution is red, and shows a fine green fluorescence.

The halogen substitution products of fluoresceïn are important dyes, and are known as the eosins (*ἑως, dawn*) from the delicate pink tints they impart to fabrics.

The tetrabromo-product, eosin proper, is obtained as a brick-red precipitate when fluoresceïn is brominated either in cold glacial acetic acid or in alkaline solution; it is purified by conversion into its potassium salt, from which it is finally liberated by dilute sulphuric acid, and extracted with ether.



(Caro, 1874), is a reddish yellow, crystalline substance, which combines with alcohol of crystallisation, but is practically insoluble in water; it dyes silk, wool and cotton (mordanted with alumina) a fine pink.

Eosin is a strong, dibasic acid, and forms stable, soluble *alkali salts*, which are known as *water-eosins*; they are used in paper-making, as the fibre is already mordanted during the sizing (§ 351), and hence readily takes up the dye without further preparation. The *mono-ethyl ester*, which is made by brominating fluoresceïn in alcoholic solution, is known as *spirit eosin*.

The *iodofluoresceïns* and *nitrofluoresceïns* are similar products; the tetriodo-compound, which is made in the same way as eosin, is known

as *erythrosin*. Fluorescein itself dyes silk and wool yellow, with a greenish fluorescence, but the colour is not fast to light; its disodium salt was at one time used as a dye, under the name of *uranin*.

*Gallein* is a blue dye, which is made from pyrogallol and phthalic anhydride; it can be converted into *carulein*, an olive-green dye derived from anthracene (§ 375). The amino-compounds corresponding with the fluoresceins (two amino- or alkylamino-groups taking the place of the phenolic hydroxy-groups) are known as *rhodamines*.

**368. Synopsis.**—By introducing alkyl or phenyl groups into the amino-groups of rosaniline and other amino-triphenylmethanes, blue, violet and green dyes are produced, the colour depending on the number and character of the groups thus introduced. The phthaleins, formed by condensing phthalic anhydride with phenols, are lactonic derivatives of hydroxy-triphenylmethanes.



## CHAPTER LXVI

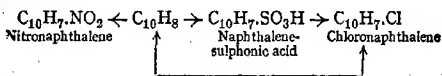
### NAPHTHALENE

**369. Naphthalene and its Halogen and Alkyl Derivatives.**—Naphthalene, the crystalline deposit which forms in gas mains during cold weather, is produced, together with benzene, etc., when the simple gaseous hydrocarbons are heated to redness; its presence in coal gas and coal tar is doubtless due to this synthesis (it is quite volatile at ordinary temperatures).

Its chief source is the middle oil of coal tar (§ 254), from which, as already stated, it crystallises on cooling; after draining under pressure, and washing away phenols with alkali, it is purified by distillation with steam, and sublimation; or it may be crystallised from alcohol.

*Naphthalene*,  $C_{10}H_8$  (Kidd, 1816; *ναφθα*=bitumen), forms large, colourless, leafy crystals, having a characteristic tarry odour; it melts at  $78^\circ$ , and boils at  $218^\circ$ , but sublimes freely at much lower temperatures, and is volatile with steam. It has marked antiseptic properties, and destroys moth and the like; but its chief use is in the manufacture of indigo and the phthalein and azo dyes.

Naphthalene resembles benzene in most of its actions, and forms chloro-, nitro-, and sulphonic substitution products even more readily, as well as comparatively unstable additive products.



The isomerism of its derivatives is much more complicated, however; two sets of mono-substitution products are known, and no less than ten (or, if the substituting groups are dissimilar, fourteen) sets of di-substitution products.

*$\alpha$ -Chloronaphthalene*,  $C_{10}H_7Cl(\alpha)$  (Laurent, 1831), a liquid boiling at  $263^\circ$ , is formed by directly chlorinating the boiling hydrocarbon, whilst the  *$\beta$ -compound*, a crystalline solid melting at  $56^\circ$ , is prepared from the

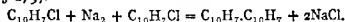
corresponding amino-compound by the diazonium interaction, or from the sulphonic acid by the action of phosphorus pentachloride (cf. § 249).

The ten *dichloronaphthalenes*,  $C_{10}H_6Cl_2$ , are crystalline substances, which are mostly prepared by indirect methods. The additive compound *naphthalene tetrachloride*,  $C_{10}H_4Cl_4$ , which is a crystalline substance melting at  $182^\circ$ , is formed by chlorination in cold chloroform, and on oxidation with nitric acid is converted into phthalic acid.

The halogen-naphthalenes closely resemble the halogen-substituted benzenes; their halogen is not displaced by boiling with alkalis, ammonia, etc. (§ 244), but, like that of the benzene derivatives, is readily exchanged for hydrocarbon radicals by the sodium method, or for hydrogen by reduction. Similarly the additive tetrachloride is converted into a substitutive dichloro-compound by partial dehalogenation with alkali.

Naphthalene further resembles benzene in forming alkyl and aryl derivatives such as the methyl-naphthalenes, phenyl-naphthalenes and dinaphthyls, which are analogous to toluene, diphenyl, etc.

The two *methylnaphthalenes*,  $C_{10}H_7CH_3$ , are liquids, which like methylbenzene, are present in coal-tar. The two *phenylnaphthalenes*,  $C_{10}H_7C_6H_5$ , and three *dinaphthyls*,  $C_{10}H_7C_{10}H_7$  ( $\alpha\alpha$ ,  $\alpha\beta$ ,  $\beta\beta$ ), are crystalline solids, which are formed synthetically; the  $\beta\beta$ -compound is made by the action of sodium on  $\beta$ -chloronaphthalene in boiling xylene in presence of ethyl acetate (§ 279).

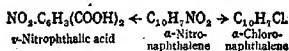


Like benzene, naphthalene forms an additive compound with picric acid, which is precipitated on mixing the alcoholic solutions of the two substances. *Naphthalene picrate*,  $C_{10}H_6C_6H_3(NO_2)_3.OH$ , is a red crystalline substance, which melts unchanged at  $149^\circ$ , but is readily decomposed into its components by alkalis, or by boiling with alcohol.

**370. The Nitro-Naphthalenes and Naphthalene-Sulphonic Acids.**—Naphthalene is nitrated as easily as benzene. On digesting it with nitro-sulphuric acid at the ordinary temperature, or better, on heating its solution in glacial acetic acid with nitric acid on a water-bath, it is converted into  $\alpha$ -nitronaphthalene, which is purified in the same way as dinitrobenzene (§ 292).

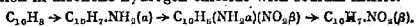
$\alpha$ -Nitronaphthalene,  $C_{10}H_7NO_2(\alpha)$  (Laurent, 1848), is a yellow crystalline substance, melting at  $61^\circ$ . It resembles nitrobenzene in most of its actions, and is reducible to the corresponding amine, naphthylamine (§ 371).

On the other hand it is oxidised by chromic acid mixture to *o-nitrophthalic acid*, a crystalline substance resembling the nitrobenzoic acids; when heated with phosphorus pentachloride it is converted into *o-chloronaphthalene*.



**$\beta$ -Nitronaphthalene**,  $\text{C}_{10}\text{H}_7\text{NO}_2(\beta)$ , a similar yellow substance melting at  $79^\circ$ , is obtained indirectly, from the  $\alpha$ -derivative, through the above amino-compound.

$\alpha$ -Naphthylamine is digested with dilute nitric acid, and the amino-group is eliminated from the resulting  $\beta$ -nitro- $\alpha$ -naphthylamine by warming its solution in alcoholic hydrogen chloride with sodium nitrite.

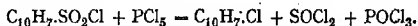


Both naphthalene-sulphonic acids are formed when the hydrocarbon is sulphonated; they are separated by fractionally crystallising their calcium salts, the  $\alpha$ -salt being much the more soluble.

At  $100^\circ$ , the  $\alpha$ -acid is the main product, but at  $160^\circ$  it is transformed into the  $\beta$ -acid, and the latter therefore predominates when the hydrocarbon is sulphonated above this temperature; the transformation is due to the successive formation and partial hydrolysis of the  $\alpha\beta$ -disulphonic acid, the  $\alpha$ -sulphonic group being eliminated the more readily (§ 247).

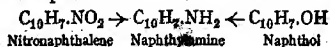
$\alpha$ - and  $\beta$ -Naphthalenesulphonic acids,  $\text{C}_{10}\text{H}_7\text{SO}_3\text{H}$  (Faraday, 1826), are deliquescent, crystalline substances, resembling benzenesulphonic acid. They are converted into *sulphonic chlorides* by phosphorus pentachloride, and these are in turn converted by ammonia into crystalline *sulphonamides*.

The naphthalene sulphochlorides differ from the benzene sulphochlorides in that they are resolved into the corresponding chloronaphthalenes by the further action of phosphorus pentachloride.



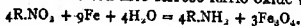
By the action of fuming sulphuric acid on naphthalene, *di*- and *tri*-sulphonic acids are formed, in the same way as with benzene.

**371. The Naphthylamines and Naphthols.**—The nitronaphthalenes are easily reduced to the corresponding naphthylamines, which are bases analogous to aniline;  $\alpha$ -naphthylamine is usually prepared in this manner. They are also formed by heating the naphthols with zinc ammoniochloride (§ 255), and the  $\beta$ -compound is conveniently made in this way; the action takes place much more readily than with phenol, and at a lower temperature.



The bases are set free by lime or soda and purified by distillation with superheated steam; or in the laboratory, by extraction with ether. The

most suitable reducing agent is iron with a little hydrochloric acid (compare Aniline, § 249); the ferrous chloride acts as a carrier, being alternately oxidised to a basic ferric chloride,  $\text{Fe}_2\text{Cl}_4\text{O}$ , and regenerated by the iron, which is converted into ferrous-ferric oxide (Witt).

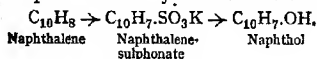


*$\alpha$ -Naphthylamine*,  $\text{C}_{10}\text{H}_7\text{NH}_2(\alpha)$  (Zinin, 1842), which is a colourless, crystalline substance of somewhat unpleasant odour, melts at  $50^\circ$ , and boils at  $300^\circ$ , but sublimes readily at a lower temperature.  *$\beta$ -Naphthylamine* is a similar crystalline substance, which melts at  $112^\circ$ , and is odourless.

The naphthylamines resemble aniline in their actions, and form diazotisable salts with acids, but their basic properties are less pronounced; their salts are decomposed by sodium carbonate (compare Naphthols, below). They are more easily oxidised than aniline, and soon turn brown in the air.

When  *$\alpha$ -naphthylamine* is boiled with chromic acid mixture, it is converted into naphthoquinone (§ 373), which on further oxidation is degraded to phthalic acid; this also is the product of the direct oxidation of  *$\beta$ -naphthylamine*. The  *$\beta$ -base* may be converted into the  *$\beta$ -nitro-compound* by the action of cuprous oxide on its diazonium nitrite, and the  *$\alpha$ -base* differs from it in yielding colouring matters with weak oxidising agents such as ferric chloride.

The naphthylamines are converted by nitrous acid into naphthols or naphthalene phenols; these compounds occur in coal tar in small quantity, but are usually made from the naphthalenesulphonic acids by fusion with alkali (§ 255).



*$\alpha$ -Naphthol*,  $\text{C}_{10}\text{H}_7\text{OH}(\alpha)$  (Griess, 1866), is a colourless, crystalline substance, having a slight phenolic odour; it melts at  $94^\circ$ , and is only sparingly soluble in water.  *$\beta$ -Naphthol* is similar, but melts at  $122^\circ$ , and is more soluble. The naphthols resemble the phenols, but are distinctly more reactive.

Whilst they are readily benzoylated (§ 270) and give coloured *ferric derivatives*, unlike phenol they are soluble in alkali carbonates, and easily convertible into amines. They also form ethers, such as *naphthyl ethyl ether*, when simply warmed with alcoholic hydrochloric acid; the  *$\beta$ -naphthyl ethers* are used in perfumery.

Like phenol, the naphthols are converted by nitric acid into yellow nitro-compounds, which are acid in character and have marked tinctorial power. The naphthylamine and naphthol-sulphonic acids are also employed technically in the preparation of dyes (§ 383); fourteen of each are theoretically possible.



*Dinitro- $\alpha$ -naphthol*,  $C_{10}H_7(NO_2)_2.OH$ , is a brilliant yellow, crystalline substance, resembling picric acid in almost every respect; its sodium salt, *Martius' yellow*, is used as a dye, and the potassium salt of its sulphonic acid is similarly used as *naphthol yellow*.

*Naphthionic* or  *$\alpha$ -naphthylaminesulphonic acid*,  $C_{10}H_6(SO_3H).NH_2(a)$ , is formed by directly sulphonating  $\alpha$ -naphthylamine at  $130^\circ$ ; it is a sparingly soluble compound which is isolated in the ordinary manner. The photographic developer, eikonogen, is an *amino- $\beta$ -naphtholsulphonic acid*.

When reduced with sodium in amyl alcohol, the naphthylamines are converted into tetrahydronaphthylamines, but whereas the  $\alpha$ -compound is comparatively little altered in properties, the  $\beta$ -compound is converted mainly into a paraffinoid amine (§ 372). The naphthols behave similarly.

*Tetrahydro- $\alpha$ -naphthylamine*,  $C_{10}H_{11}.NH_2(a)$  (Bamberger, 1889), is a neutral oily liquid which boils at  $289^\circ$ . Like  $\alpha$ -naphthylamine it can be diazotised, and is very readily oxidised; it reduces ammonio-silver solutions, and yields adipic and oxalic acids with permanganate (§ 372).

*Tetrahydro- $\beta$ -naphthylamine* (Bamberger, 1888) is an alkaline, ammoniacal liquid boiling at  $251^\circ$ ; it has no reducing action, is converted into naphthalene by nitrites in acid alcohol, and into *o-carboxyhydrocinnamic acid*,  $COOH.C_6H_4.CH_2.CH_2.COOH(o)$ , by alkaline permanganate.

The tetrahydronaphthols show analogous differences (§ 372).

Like benzene, naphthalene forms a series of carboxylic acids, alcohols, ketones, etc., and these are closely analogous to compounds of the benzyl-benzoic group.

The *cyanonaphthalenes*,  $C_{10}H_7.CN$ , are crystalline substances which are prepared from the naphthylamines by the diazonium method; they are converted by pyrosulphuric acid into the corresponding *naphthamides*,  $C_{10}H_7.CONH_2$ , crystalline substances from which the naphthoic acids are obtained by the ordinary hydrolysis, or the action of nitrous acid.

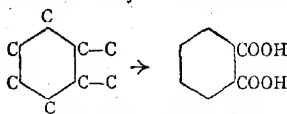
$\alpha$ - and  $\beta$ -*Naphthoic acids* are crystalline substances, which are resolved into carbon dioxide and naphthalene when distilled with lime; the  $\alpha$ -acid is the stronger ( $K_a = 0.0197$ ,  $K_p = 0.0052$ ).

*Naphthalic acid*,  $C_{10}H_6(COOH)_2$ , one of the ten naphthalene-dicarboxylic acids, is formed by oxidising *acenaphthene* or *aa-ethylenenaphthalene*,  $C_{10}H_6.C_2H_4$ , a crystalline coal-tar hydrocarbon, obtained synthetically by debrominating *o-bromo- $\alpha$ -ethylnaphthalene*,  $C_{10}H_7.CH_2.CH_2.Br$ . As naphthalic acid readily forms an *anhydride*, and is not the known  $\alpha\alpha$  or  $\alpha\beta$ -acid, the carboxyl groups are in the *aa* or *peri*-position (§ 372).

**372. Constitution of Naphthalene.**—The close analogy between naphthalene and benzene leaves little doubt as to its benzenoid constitution, which moreover is decisively proved by its oxidation to phthalic acid (§ 324), when boiled with nitric acid.

The same oxidation is carried out technically with hot, concentrated sulphuric acid in presence of mercuric sulphate; for laboratory purposes it is conveniently effected by oxidising naphthalene tetrachloride (§ 369), or the crude dichloride (which is obtained by heating the hydrocarbon with hydrochloric acid and potassium chlorate) with nitric acid.

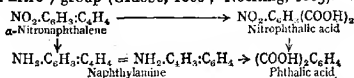
This oxidation not only proves that naphthalene is a benzene derivative, but also indicates that two of the additional carbon atoms are linked in the ortho-position, whilst the remaining pair are not directly connected with the ring.



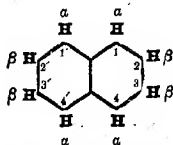
Benzenoid Nucleus of Naphthalene.

The four additional atoms cannot form an open chain, or the additive chloride would be a hexachloride; they must therefore form another ring. The complete analogy between benzene and naphthalene indicates that this also is a benzene ring (Erlenmeyer, 1866).

The correctness of the inference is proved by the different behaviour of  $\alpha$ -nitronaphthalene and  $\alpha$ -naphthylamine when oxidised; whilst the nitro-compound yields nitrophthalic acid (§ 370), the amine obtained by reducing it gives phthalic acid itself. This result is only intelligible on the assumption that there is a benzene ring in the amino-molecule (and therefore in the nitro-molecule), distinct from that which contains the amino- (and nitro-) group (Graebe, 1880; Noeltling, 1883).



The naphthalene molecule thus consists of two benzene rings, which have two adjacent carbon atoms in common; its nucleus is a condensed benzene ring. This result affords an independent proof of the orientation of phthalic acid.

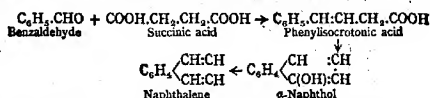


Structural Formula of Naphthalene  
( $\alpha$ ,  $\alpha'$ ,  $\beta$ ,  $\beta'$  are sometimes numbered 8, 7, 6, 5; 1, 8 = *peri*-position)

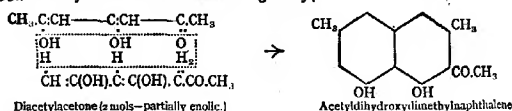
The above formula is confirmed by the synthesis of naphthalene from benzaldehyde and succinic acid.

On heating these substances with sodium succinate, they condense, losing water and carbon dioxide (compare § 332), and on boiling the crystalline product, *phenylisocrotinic acid*, either alone or with water, it

suffers further condensation to  $\alpha$ -naphthol; this is converted into the hydrocarbon by distillation with zinc dust (Fittig, 1883).



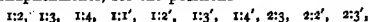
A direct synthesis of a naphthalene derivative from an open-chain compound is afforded by condensing diacetylacetone (§ 409) with itself, in slightly alkaline solution, orcinol (§ 302) being formed at the same time. *Acetyl-dihydroxy-dimethylnaphthalene*,  $\text{CH}_3\cdot\text{CO}\cdot\text{C}_{10}\text{H}_8\text{Me}_2(\text{OH})_2$  (Collie, 1893), is a crystalline substance melting at  $194^\circ$ .



The best justification of the formula, however, is the agreement of the isomerism of the naphthalene substitution-products with that which is required by theory. An exhaustive examination of the chloro-derivatives of naphthalene, prepared in all possible ways, has shown that all the required compounds can be made, and that there are no others (Armstrong, Wynne, 1890-1895); there are two chloronaphthalenes, ten dichloronaphthalenes, and fourteen trichloronaphthalenes.

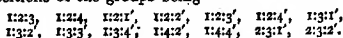
There should be two sets of monosubstitution products, for the positions next the central carbon atoms ( $\alpha$ ) are differently situated from the other four ( $\beta$ ).

Similarly, there should be ten sets of di-substitution products, such as the dichloronaphthalenes, for the positions



are all different.

Finally, there should be fourteen trichloro- or similar products, the respective positions of the groups being—



The double ring formula also explains the difference between the reduced naphthylamines (§ 371); tetrahydro- $\alpha$ -naphthylamine is an analogue of aniline, whilst the corresponding  $\beta$ -naphthylamine product is derived from aminocyclohexane.

The general resemblance of the  $\alpha$ -compound to the aromatic amines shows that the amino-substituted ring is still essentially aromatic, and unreduced; the  $\alpha$ -compound is therefore termed aromatic or *ar-tetrahydro- $\alpha$ -naphthylamine*. The highly basic nature of the  $\beta$ -amine, on the other hand, shows that it is aliphatic in character, and that the hydrogen is combined with the amino-substituted ring; the  $\beta$ -compound

is therefore termed alicyclic or *ac*-tetrahydro- $\beta$ -naphthylamine. The related naphthol derivatives show similar differences; *ar*-tetrahydro- $\alpha$ -naphthol is a crystalline substance (m.p. 69°) which resembles phenol rather than naphthol, whilst *ac*-tetrahydro- $\beta$ -naphthol is a liquid alcohol (b.p. 266°) of cycloparaffinoid type.

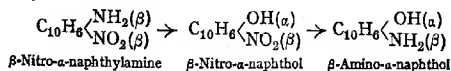
The marked difference between the naphthylamines and naphthols, and their *ar*-reduction products, would seem to indicate that the molecule of naphthalene itself contains only one ring, with ten centric valencies (Bamberger, 1890; see Quinoline, § 389).

**373. The Naphthoquinones.**—When  $\alpha$ -naphthylamine is boiled with chromic acid mixture it is converted into  $\alpha$ -naphthoquinone, which, however, is more conveniently prepared by oxidising the hydrocarbon itself with chromic anhydride in glacial acetic acid; it is isolated by distillation with steam.

$\alpha$ -Naphthoquinone,  $C_{10}H_6 \begin{smallmatrix} \text{CO} \cdot \text{CH} \\ \text{CH} \cdot \text{CO} \end{smallmatrix}$  (Groves, 1873), is a yellow, crystalline substance, melting at 125°, which resembles ordinary benzoquinone in appearance and odour, and in the readiness with which it sublimes.

Like quinone, it is reduced by sulphurous acid to the corresponding hydroxy-compound, 1:4-dihydroxynaphthalene, a crystalline substance resembling quinol; but it is oxidised to phthalic acid by prolonged boiling with chromic acid mixture.

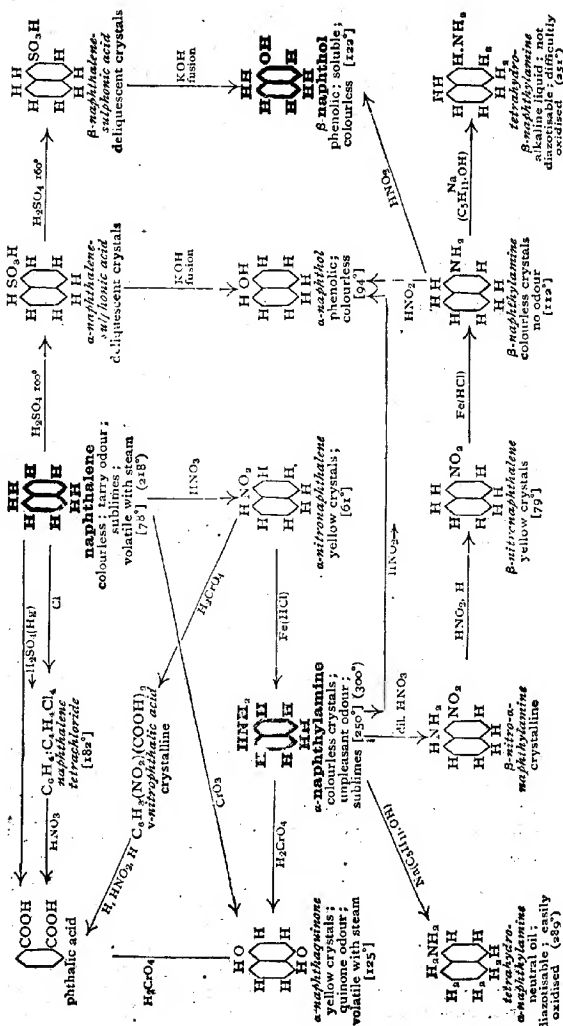
A second naphthoquinone is formed by similarly oxidising  $\beta$ -amino- $\alpha$ -naphthol, which is formed from  $\beta$ -nitro- $\alpha$ -naphthylamine (§ 370) by the successive action of nitrous acid and tin and hydrochloric acid.



$\beta$ -Nitro- $\alpha$ -naphthylamine     $\beta$ -Nitro- $\alpha$ -naphthol     $\beta$ -Amino- $\alpha$ -naphthol

$\beta$ -Naphthoquinone,  $C_{10}H_4 \begin{smallmatrix} \text{CO} \cdot \text{CO} \\ \text{CH} \cdot \text{CH} \end{smallmatrix}$ , is a red, inodorous, crystalline substance, which blackens and decomposes when heated, and does not melt or sublime, nor volatilise with steam (compare *o*-Benzoquinone, § 304); it is reduced by sulphurous acid in a similar manner to the  $\alpha$ -compound. The para-formula of the  $\alpha$ -quinone follows from its oxidation to phthalic acid, and its analogy to benzoquinone; and as the  $\beta$ -compound is also convertible into phthalic acid, it must be represented by the alternative ortho-quinone formula.

**374. Synopsis.**—Naphthalene is a hydrocarbon, which resembles benzene and forms similar derivatives, but as its molecule consists virtually of two benzene rings having two carbon atoms in common, the isomerism of its substitution products is more complex.



## CHAPTER LXVII

### ANTHRACENE AND ANALOGOUS HYDROCARBONS

**375. Anthracene and Anthraquinone.**—The "green oil" of coal tar, which passes over at  $300\text{--}350^\circ$ , and constitutes about 20 per cent. of the tar, contains a hydrocarbon anthracene, which crystallises in an impure state on cooling.

After pressing and washing with light naphtha, this commercial product contains about half its weight of the pure hydrocarbon, together with phenols and phenanthrene (§ 378). To eliminate these, it is distilled with solid potash, washed with carbon bisulphide to remove phenanthrene, and finally recrystallised from benzene until its melting point is constant.

*Anthracene*,  $\text{C}_{14}\text{H}_{10}$  (Dumas, 1832; ἀνθραξ=coal), is a colourless, but fluorescent, crystalline substance, which melts at  $217^\circ$ , and boils at  $351^\circ$ . It resembles naphthalene and benzene in most respects, forms a red, crystalline *picrate*, and can be chlorinated and sulphonated.

With chlorine at  $100^\circ$ , it yields a *chloranthracene*,  $\text{C}_{14}\text{H}_9\text{Cl}$ , and *dichloranthracene*,  $\text{C}_{14}\text{H}_8\text{Cl}_2$ , whilst in the cold, especially on chlorination in carbon bisulphide solution, it forms an additive compound, *anthracene dichloride*,  $\text{C}_{14}\text{H}_{10}\text{Cl}_2$ ; all these are crystalline products.

On heating anthracene with nitric acid under ordinary conditions, it is not nitrated, but oxidised to its quinone, anthraquinone; this substance, which is of technical importance, is more conveniently obtained by the action of chromic anhydride on a solution of the hydrocarbon in glacial acetic acid (or technically, with chromic acid mixture).

A vigorous action ensues, and on pouring the green product into water after boiling in a reflux apparatus for an hour, the anthraquinone separates as a yellow precipitate, which is washed with caustic soda and water, and purified by sublimation.

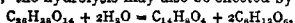
*Dinitranthracene*,  $\text{C}_{14}\text{H}_8(\text{NO}_2)_2$ , is obtained by the action of cold nitric acid (free from nitrous acid) on the hydrocarbon; it is converted into anthraquinone by hot nitric acid.

*Anthraquinone*,  $\text{C}_{14}\text{H}_8\text{O}_2$  (Laurent, 1834), is a bright yellow,



**376. Alizarin.**—The chief interest of anthracene and anthraquinone lies in their relation to alizarin, the essential constituent of madder, which is one of the most important and longest known of the natural dye-stuffs of the East.

Alizarin occurs in the madder root as a crystalline glucoside, *ruberythric acid*,  $C_{26}H_{28}O_{14}$ , and on macerating the root with water this is hydrolysed by an accompanying enzyme to glucose and the dye, which may be purified by sublimation; the hydrolysis may also be effected by dilute acids.



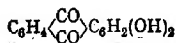
*Alizarin*,  $C_{14}H_8O_4(OH)_2$  (Rochleder, 1870), is a red crystalline substance, which melts at  $290^\circ$ , and sublimes easily; it is scarcely soluble in water, but dissolves in alkalies to a purple solution, from which insoluble, highly coloured salts, the lakes, are precipitated by metallic hydroxides; the *aluminium* and *stannic salts* are crimson, the *ferrie salt* dark violet, and the *chromic salt* purple brown.

By mordanting fabrics with the hydroxides these lakes can be precipitated within the fibres, and very fast and brilliant dyes obtained.

On steaming a fabric soaked in aluminium acetate, the salt is dissociated, and on passing the fabric, thus mordanted with alumina, through hot water in which alizarin is suspended, it is dyed a fast purple-red. In Turkey-red dyeing, by which a brilliant scarlet is produced on cotton, the fabric is mordanted with the aluminium salt of *ricinoleic acid* (hydroxy-oleic acid), which occurs as a glyceride in castor-oil. All "acid" dyes are mordanted with hydroxides in this manner.

**377. Constitution and Synthesis of Alizarin.**—From the formation of the above salts, it follows that alizarin is either an acid or a phenol; and that it is a phenol, and not an acid, is proved by its conversion by acetic anhydride into a *diacetate*, which no longer forms such salts. There remain two oxygen atoms to be accounted for.

On distilling the dye with zinc dust in a current of hydrogen, it is reduced to anthracene, and as anthraquinone is itself reduced in an identical manner, and all phenols yield their hydrocarbon when treated in this way, it follows that alizarin is *dihydroxyanthraquinone*, a diphenol of anthraquinone (Graebe, 1868).

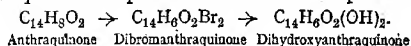


Structural Formula of Alizarin as Dihydroxyanthraquinone.

This inference is fully confirmed by synthesis; the potassium

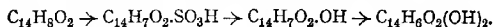


salt of alizarin is produced when either dibromanthraquinone or anthraquinonedisulphonic acid is fused with potash.



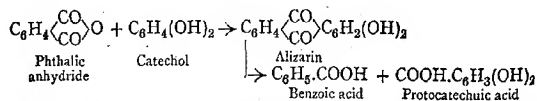
*Dibromanthraquinone*,  $\text{C}_6\text{H}_4(\text{CO})_2\text{C}_6\text{H}_2\text{Br}_2$ , is a crystalline substance, which is formed when anthraquinone is brominated at  $160^\circ$  in presence of iodine. When fused with potash (§ 255), it exchanges its halogen for hydroxyl in the normal manner (compare §§ 244, 305), and is converted into a purple potassium salt. This is identical with *potassium alizarin*, and when decomposed by acids in aqueous solution yields a red precipitate which sublimes in red crystals, and is in every respect identical with natural alizarin (Graebe, 1868).

Alizarin paste is now usually made from the sodium monosulphonate by a modification of this process, and as thus synthesised has practically supplanted the natural dye.



The crude anthraquinone, prepared by oxidising crude anthracene with chromic acid mixture, is converted into the *monosulphonic acid* by heating with fuming sulphuric acid at  $180^\circ$ ; and on fusing the sparingly soluble *sodium sulphonate* (which is termed silver salt, technically, from its lustrous appearance) with caustic soda and potassium chlorate, *sodium alizarin* is obtained, from which the dye is precipitated with dilute sulphuric acid.

On fusing alizarin with potash at a high temperature, it resolved into benzoic and protocatechuic acids, so that the phenolic groups are in the same benzene ring, and in the ortho-position relatively to one another. A similar proof is afforded by the synthesis of the dye by heating a mixture of catechol and phthalic anhydride with sulphuric acid.



The corresponding *trihydroxyanthraquinones* are formed by oxidising alizarin with manganese dioxide and dilute sulphuric acid, or by fusing anthraquinone-disulphonic acid with potash (hydrogen being evolved, as in the oxidation of resorcinol). They are also used as dyes, and produce yellower reds than alizarin; the vicinal compound, *purpurin*, is associated with it as a glucoside in madder.

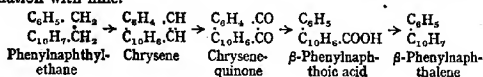
The tinctorial power of the hydroxyanthraquinones is dependent on the relative positions of the phenolic groups, for the isomeric *quinazarin* (from quinol) has no value as a dye; only those hydroxyanthraquinones have dyeing power, which contain two adjacent hydroxyl groups.

**378. Phenanthrene, Chrysene, and Picene.**—The isomeric hydrocarbon, phenanthrene, which is present in crude anthracene, is freely soluble in the carbon bisulphide used in the purification of the latter, and can be recovered from the mother-liquor; it is also formed as a bye-product in the preparation of mercury in Idria.

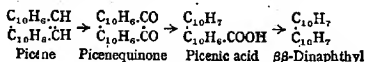
resin; when heated with hydriodic acid and phosphorus, it is reduced to *dodekahydrotene*,  $C_{18}H_{30}$ , a liquid of high boiling-point, which is also obtained by reducing abietene (§ 351) in a similar manner.

Chrysene and picene, the phenylnaphthyl and dinaphthyl compounds corresponding with phenanthrene, are obtained from the less volatile portions of coal tar and from pitch; they are characterised by their great stability at high temperatures.

*Chrysene*,  $C_{18}H_{12}$ , a colourless, fluorescent substance, which melts at  $250^{\circ}$  and boils at  $448^{\circ}$ , is also formed synthetically by distilling phenylnaphthylethane. On oxidation it yields *chrysenequinone* and  $\beta$ -phenylnaphthoic acid, the latter of which is converted into  $\beta$ -phenylnaphthalene on distillation with lime.

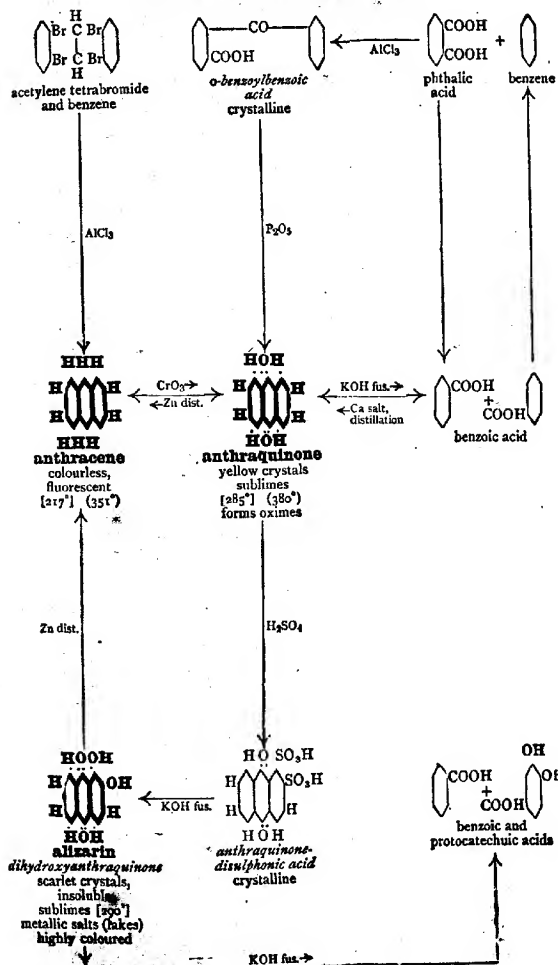


*Picene*,  $C_{22}H_{14}$ , has the highest melting point,  $364^{\circ}$ , of all the hydrocarbons, and boils only at a dull red heat. It behaves on oxidation in the same way as chrysene, being converted into *picenequinone* and *picenic* or  $\beta$ -naphthyl-naphthoic acid, from which  $\beta\beta$ -dinaphthyl (§ 369), is obtained by distillation with lime. Picene is thus the phenanthrene of the naphthalene series.



**379. Synopsis.**—Anthracene, phenanthrene, chrysene and picene are coal tar hydrocarbons which resemble naphthalene, but contain three or more benzene rings in their molecules. Anthracene is the mother substance of the natural dye alizarin, which is made synthetically from it.

## ANTHRACENE AND ALIZARIN.



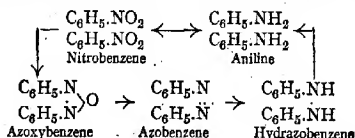
## CHAPTER LXVIII

### THE AZO-COMPOUNDS

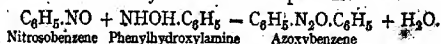
**330. Azoxybenzene, Azobenzene, and Hydrazobenzene.**—The graduated reduction of nitrobenzene to aniline, which under suitable conditions can be traced successively through nitroso-benzene and phenylhydroxylamine (§ 263), becomes further complicated when the action takes place at a higher temperature, and especially in presence of alkalis.

The initial product in such actions is azoxybenzene; but when a somewhat more energetic agent is employed, such as zinc dust and alkali, sodium amalgam, or alkaline stannite, this product is further reduced to azobenzene and hydrazobenzene, either of which may be isolated, according to the conditions.

By still more energetic reduction, especially in acid solution, these various compounds are resolved into aniline, so that the three reduction products form a second series of connecting links between nitrobenzene and its amino-derivative.



Azoxybenzene is prepared by boiling nitrobenzene in a reflux apparatus with alcoholic sodium methoxide (sodium in methyl alcohol); it probably results from the condensation of the nitroso- and hydroximino-compounds.



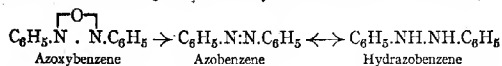
When after some hours' boiling, the odour of the nitro-compound can no longer be detected, the solvent is distilled off; the solid residue is then

washed with water, to remove the sodium formate which results from the oxidation of the methoxide, and the yellow azoxybenzene is recrystallised from dilute alcohol (§ 244) or light petroleum.

*Azoxybenzene*,  $\text{C}_6\text{H}_5\cdot\text{N}_2\text{O}\cdot\text{C}_6\text{H}_5$  (Zinin, 1845), is a bright yellow, crystalline substance, which melts at  $36^\circ$ , and is indifferent to acids and alkalis; when distilled with reduced iron, or even when rapidly heated, it is reduced to azobenzene, and it is similarly converted into the azo- and hydrazo-compounds by reduction with zinc and alkali.

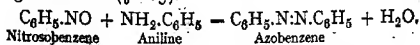
Azoxybenzene is resolved into aniline when reduced with zinc and acetic acid, and is converted into the isomeric hydroxyazobenzene (§ 382) by the action of concentrated sulphuric acid.

Both azobenzene and hydrazobenzene may be obtained by adding zinc dust to a warm alcoholic solution of nitrobenzene, containing caustic soda; the action is energetic, and should be moderated by cooling if necessary. If the addition of zinc is discontinued immediately the odour of nitrobenzene has disappeared, the liquid is deep orange in colour, and the product mainly azobenzene, whilst by further addition of the metal to the boiling solution, hydrazobenzene is obtained.



The azo-compound is in part formed by the reduction of azoxybenzene, and may be obtained, with good yield, by distilling this compound with reduced iron. Its formation is also due, however, to oxidation of the hydrazo-compound by unchanged nitrobenzene; it may thus be prepared almost quantitatively from the nitro-compound, by reducing it electrolytically in alkaline alcoholic solution, with an electromotive force below that which is required to reduce the hydrazobenzene to aniline (compare § 263); some azoxybenzene is regenerated during the oxidation of the hydrazo-compound by the nitro-compound, but is again reduced to the hydrazo-compound as the action continues.

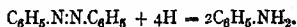
Azobenzene is also formed in small quantity by the action of oxidising agents, such as hypobromites, on aniline; the brick-red precipitate obtained with sodium hypobromite (§ 249) consists mainly of this compound. Its formation is here probably due to the condensation of nitrosobenzene with unchanged aniline (§ 263).



The hydrazobenzene is isolated from the above alcoholic product by pouring the colourless filtrate into water, and recrystallising the precipitate from alcohol. The azobenzene may be obtained by simply concentrating

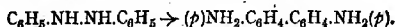
the intermediate orange solution, but as it is difficult to stop the reduction exactly at the right stage, it is better to complete it, and then oxidise the crude hydrazobenzene by passing nitrous fumes into the filtered alcoholic solution, or boiling it with solid ferric chloride. Practically, however, the reduction of azoxybenzene with iron gives the most satisfactory results.

*Azobenzene* or *benzene-azobenzene*,  $C_6H_5.N:N.C_6H_5$  (Mitscherlich, 1834), is an orange-red, crystalline substance, which melts at  $68^\circ$ , and at  $293^\circ$  boils to a deep red vapour; it has a faint, fragrant odour. It is chemically indifferent, and combines neither with acids nor alkalies; but on further reduction, as with zinc dust and acetic acid, is resolved into aniline.



*Hydrazobenzene* or *symmetrical diphenylhydrazine*,  $C_6H_5.NH.NH.C_6H_5$  (Hofmann, 1863), is a colourless, crystalline substance, which melts at  $131^\circ$ . Like azobenzene, it is indifferent to acids and alkalies, and is reduced to aniline by zinc dust and acetic acid, but it is less stable than the coloured product, and is readily reoxidised to it, even by air.

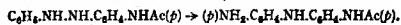
Itself indifferent, hydrazobenzene is converted by simple digestion with concentrated hydrochloric acid into a basic isomeride, *benzidine* or *p-diaminodiphenyl* (§ 353).



Benzidine transformation.

The same transformation is effected by reducing alcoholic azobenzene with tin and hydrochloric acid, the hydrazobenzene at first formed at once undergoing conversion; after distilling off the alcohol, the sparingly soluble benzidine sulphate is precipitated with dilute sulphuric acid, and the base separated with ammonia.

The homologous compounds derived from the nitrotoluenes, etc., are transformed in a similar manner, except when one or both para-positions are already occupied, in which case only one of the benzene nuclei is turned round, and derivatives of diphenylamine are formed; these isomerisations are known respectively as the benzidine and semidine transformations.



Semidine transformation

The constitution of azobenzene rests partly on its relation to nitrobenzene, nitrosobenzene, phenylhydroxylamine and aniline, and partly on the synthesis of its derivatives from diazonium compounds (below).

**381. Aminoazobenzene: Colour of Azo-Compounds.**—The azo-compounds are the mother substances of a large class of valuable dyes. Although azobenzene is itself intensely coloured, it is useless as a dye, for being indifferent to acids

and bases it combines neither with fibres nor mordants, and cannot be made fast in the fabric.

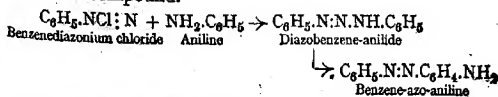
By introducing salt-forming acid or basic groups, however, such as hydroxyl and amidogen, derived products are obtained, which are still highly coloured, but now, like indigo and the rosanilines, form stable combinations with mordants, etc., and can be fixed permanently in the fibre; these are the azo-dyes.

Radicals such as the azo- and nitro-groups, which confer colour on a chromogenic molecule (§ 366) such as that of benzene, or more correctly, render its latent colour visible, are termed chromophores (Witt, 1876); their special property is attributable in the great majority of cases to the readiness with which they lend themselves to the transformation of the chromogenic molecule into a quinonoid form (§ 362).

In the case of the triphenylmethane dyes, the amino-group which constitutes the chromophore is also the salt-forming group which converts the colouring matter into a dye, but this coincidence is not essential, and in the azo-dyes the salt-forming radical (which is sometimes termed the auxochrome) is distinct from the chromophoric azo-group.

The selective absorption of light to which the colour of substances is due is by no means confined to the visible spectrum, and many chromogenic compounds, such as benzene, show extensive absorption in the ultra-violet region, beyond the limits of visibility. Such chromogens must therefore logically be classed with coloured substances, the invisibility of the colour being due merely to physiological limitations. Chromogens are thus invisibly coloured substances, and chromophores are atoms or groups which are capable of reducing the rate of vibration of the chromogenic molecule, so that it absorbs light of ordinary refrangibility (Hartley 1886).

Aminoazobenzene, the prototype of the azo-dyes, was first obtained by the action of nitrous fumes on alcoholic aniline (Mène, 1861), its oxalate being used as a dye, under the name of *aniline yellow* (Nicholson, 1863). Its formation involves the diazotisation of part of the aniline, and consequent production of diazobenzene-anilide (§ 259), and like most diazonium interactions is materially facilitated by generating the nitrous acid in the solution; in the presence of excess of the aniline salt, the diazobenzene-anilide is converted into the aminoazo-compound.



A concentrated solution of sodium nitrite is added with the usual precautions (§ 260) to a solution of aniline hydrochloride in the requisite amount of warm aniline. The product, which now contains diazobenzene-



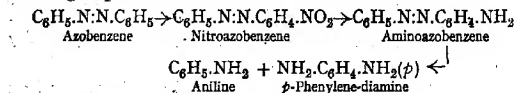
anilide, formed by the interaction of the diazonium chloride with part of the aniline, is kept warm until the transformation of the anilide is complete, and no nitrogen is evolved on warming a small portion with concentrated hydrochloric acid. The amino-azobenzene and unchanged aniline are next dissolved in concentrated hydrochloric acid, and kept at 60–70°; the yellow azo-hydrochloride is slowly precipitated, and after washing with dilute hydrochloric acid, is decomposed with ammonia, the free base being crystallised from benzene and alcohol.

*Aminoazobenzene* or *benzene-azo-aniline*,  $C_6H_5.N:N.C_6H_4.NH_2$  (Griess, 1866), which is an orange, crystalline substance having a blue reflex, melts at 126°; its *oxalate*, aniline yellow, is a steel-blue crystalline substance, which dissolves in water to a yellow solution.

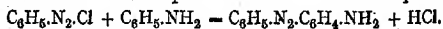
Aniline yellow dyes silk and wool directly, but cotton only after mordanting with stannic tannate (§ 360); the colour is a dull and fugitive yellow, but a purer and faster colour, *acid yellow*, is given by the sodium salt of the corresponding *sulphonic acid*.

Aminoazobenzene is now manufactured chiefly for conversion into dark blue dyes, the *indulines*, complex substances which are made by heating the azo-compound with aniline hydrochloride and aniline.

The constitution of this base is confirmed by its production from *nitroazobenzene*, by reduction with ammonium sulphide, and by its resolution into aniline and *p*-phenylenediamine, when reduced with stannous chloride; the orientation of the amino-group also follows from the latter interaction.



**382. Benzene Azo-Dyes.**—The azo-dyes are made almost exclusively by means of the diazonium interaction, the possibilities of which in this respect are very great. The net result of the interaction of benzenediazonium chloride with aniline is the introduction of the benzenediazo-radical in the para-position to the amino-group of the aniline; the diazotised amine is said to be coupled with the second compound.



Coupling of Benzenediazonium Chloride with Aniline.

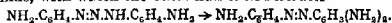
Such coupling can be effected between practically any diazotised amine and any aminic or phenolic compound, subject only to the limitation that a para-position is free in the second molecule; the intervention of a diazoanilide is not essential, and often impossible, as for example with dimethylaniline. Substituted anilines such as sulphanilic acid are also

readily diazotised, so that sulphonated and other substituted azo-compounds can be made directly by this method.

Meta-azo-compounds, however, in which the azo-group is in the meta-position to the amino- or other radical, cannot be made by direct coupling, and ortho-azo-compounds but rarely.

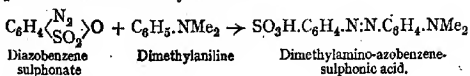
By thus introducing more amino-groups into the azobenzene molecule, browner tints are obtained, whilst with alkylated amino-groups the colour is shifted towards the red end of the spectrum.

Diamino-azobenzene is made from the benzenediazonium salt and meta-phenylene-diamine, whilst the triamino-compound is formed by the direct action of nitrous acid on the latter diamine, half being converted into the diazo-anilide, with which the other half then interacts.



*Benzene-azo-m-phenylenediamine* or *chrysoidine*,  $\text{C}_6\text{H}_5\cdot\text{N}\cdot\text{N}\cdot\text{C}_6\text{H}_3(\text{NH}_2)_2$  (Witt, 1877), is a deep red, crystalline substance, which dyes silk and wool yellow, and cotton (mordanted with tannin) a dark yellow. *m-Aminobenzene-azo-metaphenylenediamine*,  $\text{NH}_2\cdot\text{C}_6\text{H}_4\cdot\text{N}\cdot\text{N}\cdot\text{C}_6\text{H}_3(\text{NH}_2)_2$  (Caro, Griess, 1867)—Bismarck or Manchester brown—is a brown crystalline substance, which dyes leather and mordanted cotton a dark brown.

The alkylamino-azobenzenes are similarly formed by the direct action of diazonium salts on alkyl-anilines; the formation of an intermediate diazo-anilide is here impossible, as both amino-hydrogen atoms are replaced. The well-known indicator, methyl orange, is thus made from benzenediazonium-sulphonate and dimethylaniline.



The sulphonate is made by diazotising sodium sulphanilate, and after adding the solution of the amine hydrochloride, followed by a slight excess of alkali, the azo-compound can be precipitated with salt.

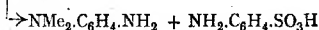
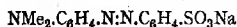
*Methyl orange* or *sodium p-dimethylaminobenzene-azobenzene-sulphonate*,  $\text{NMe}_2\cdot\text{C}_6\text{H}_4\cdot\text{N}\cdot\text{N}\cdot\text{C}_6\text{H}_4\cdot\text{SO}_3\text{Na}$  (Griess, 1877), is an orange, crystalline powder, which dissolves in water to a yellow solution; the free acid is intensely red in colour.

As a very minute amount of the sulphonic acid is perceptible in solution, and is practically decolorised by a corresponding trace of alkali, methyl orange forms a valuable indicator in alkalimetry (Lunge, 1878); it is especially useful as the acid is a fairly strong acid, and is not set free by

carbonic or hydrosulphuric acids, nor as a rule by acid salts. Methyl orange is not used as a dye on account of this sensitiveness.

The constitution of methyl orange is confirmed by its reduction to sulphanilic acid and *p*-aminodimethylaniline, when a solution of stannous chloride in hydrochloric acid is added to its hot concentrated solution; the sulphanilic acid crystallises out, and the diamine is liberated from the residue with caustic soda, and extracted with ether.

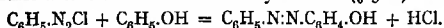
The constitution of all azo-compounds is determined by such reduction, which also indicates the method of formation; chrysoidine thus yields aniline and *as-triaminobenzene*.



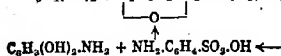
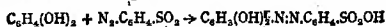
Determination of the Constitution of an Azo-Dye.

The hydroxy-azobenzenes or tropæolines are made in the same way as the aminoazo-compounds; the diazotised solution is slowly added to the cold, slightly alkaline solution of the phenol, and the product precipitated with salt.

*Benzene-azo-phenol* or *hydroxyazobenzene*,  $\text{C}_6\text{H}_5 \cdot \text{N} : \text{N} \cdot \text{C}_6\text{H}_4 \cdot \text{OH}$  (Griess, 1876), an orange, crystalline substance, which melts at  $154^\circ$ , is made by coupling diazotised aniline with phenol in alkaline solution; it is also formed by the action of hot sulphuric acid on the isomeric azoxybenzene (§ 380).

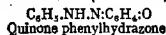
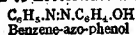


The dye-stuff *tropæolin O* or *chrysoin*, a yellowish-red, crystalline substance, which dyes silk and wool deep yellow (when acidified), is *sodium resorcinol-azo-benzenesulphonate*  $\text{C}_6\text{H}_3(\text{OH})_2 \cdot \text{N} : \text{N} \cdot \text{C}_6\text{H}_4 \cdot \text{SO}_3\text{Na}$ ; it is made by coupling diazotised sulphanilic acid with alkaline resorcinol, or by sulphonating the corresponding *benzene-azo-resorcinol*, made from diazotised aniline; when reduced with tin and hydrochloric acid, it is resolved into *aminoresorcinol* and sulphanilic acid;

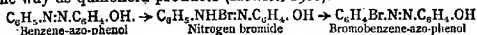


While in most of their actions the azophenols undoubtedly act as true phenols, they behave with certain substituting agents as if they were derivatives of quinone-phenylhydrazone. When hydroxyazobenzene is nitrated with dilute nitric acid, it is converted into *benzene-azo-o-nitrophenol*,  $\text{C}_6\text{H}_3 \cdot \text{N} : \text{N} \cdot \text{C}_6\text{H}_3(\text{NO}_2) \cdot \text{OH}$ , a yellow, crystalline substance, which like *o*-nitrophenol, forms red alkali salts. With concentrated nitrosulphuric acid, on the other hand, it yields *p-nitrobenzene-azo-phenol*,  $\text{NO}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{N} : \text{N} \cdot \text{C}_6\text{H}_4 \cdot \text{OH}$ , the formation of which must apparently be preceded by that of a *nitramine*,  $\text{C}_6\text{H}_5 \cdot \text{N}(\text{NO}_2) \cdot \text{N} \cdot \text{C}_6\text{H}_4 \cdot \text{O}$  (§ 359).

The first action points to an azophenolic structure, whilst the second would appear to necessitate a quinonoid structure (Hantzsch, 1899).



These apparently contradictory conclusions are reconciled by a study of the bromination products of the hydroxyazo-compound. When the eliminated hydrogen bromide is allowed to accumulate, *bromobenzene-azo-phenol* is formed, whilst when it is removed by the addition of sodium acetate, *benzene-azo-bromophenol* is obtained. The pseudo-quinonoid behaviour of benzene-azo-phenol is therefore due to the presence of the mineral acid, the resulting quinquevalence of the nitrogen causing it to yield transitory ammonium bromides (cf. § 252), which behave in the same way as quinonoid products (Hewitt, 1900).



**383. Naphthalene Azo-Compounds.**—Naphthalene forms azo-compounds of the same character as those of benzene, the azo-group in some cases being linked to two naphthyl radicals, and in others to a naphthyl and a benzenoid radical.

On passing nitrous anhydride into  $\alpha$ -naphthylamine, the naphthalene-diazonium nitrite interacts with a further quantity of the base, just as with aniline, forming *diazonaphthalene-naphthylamide*, an unstable crystalline substance resembling the corresponding benzene compound; and when this is heated with naphthylamine, it is similarly transformed into amino-azonaphthalene or naphthalene-azo-naphthylamine.

*Naphthalene-azo-naphthylamine*,  $\text{C}_{10}\text{H}_7\cdot\text{N}:\text{N}:\text{C}_{10}\text{H}_6\cdot\text{NH}_2$ , is a brownish-red, crystalline substance; its *sulphonic acids*, which are formed from the naphthylamine sulphonic acids, are used as dyes.

Diazotised amines couple exceedingly easily with alkaline  $\beta$ -naphthol, which can therefore be used as a test for diazonium compounds and diazotates; an immediate red or yellow precipitate of an azo-compound is obtained if such be present.

*Roccellin* or sodium  $\beta$ -naphthol-azo-naphthalenesulphonate,  $\text{SO}_3\text{Na}\cdot\text{C}_{10}\text{H}_6\cdot\text{N}:\text{N}:\text{C}_{10}\text{H}_6\cdot\text{OH}$ , which is formed by coupling diazotised naphthionic acid with  $\beta$ -naphthol, is a red dye which has largely supplanted natural cochineal; the mixed azo-compound, *Orange II*,  $\text{SO}_3\text{Na}\cdot\text{C}_6\text{H}_4\cdot\text{N}:\text{N}:\text{C}_{10}\text{H}_6\cdot\text{OH}$ , made by coupling  $\beta$ -naphthol with diazotised sulphanilic acid, is a deep yellow dye.

Pure red dyes are obtained by the action of alkylbenzene-diazonium compounds on the naphthylamines and their derivatives; the scarlet dye, "*Ponceau 2R*,"  $\text{C}_6\text{H}_5\text{Me}_2\cdot\text{N}:\text{N}:\text{C}_{10}\text{H}_4(\text{SO}_3\text{Na})_2\cdot\text{OH}$ , is thus made from xylenediazonium chloride and  $\beta$ -naphtholsulphonic acid. Many such dyes are manufactured, of all shades from brown to scarlet.

**384. Bisazo or Tetrazo-Compounds.**—The simple azo-dyes are fast only on mordanted cotton, but more complex compounds

have been made which dye vegetable fibres directly, and are therefore termed substantive dyes, as distinguished from the mordanted or adjective dyes; they all contain two azo-groups, and many of them are made from benzidine.

When benzidine is diazotised, it forms a double diazonium-compound, *diphenyl-bisdiazonium chloride*,  $\text{N} \equiv \text{N} \cdot \text{C}_6\text{H}_4 \cdot \text{C}_6\text{H}_4 \cdot \text{N} \equiv \text{N} \cdot \text{Cl}$ , and this couples with phenols, etc., in the same way as the simple diazonium salts, but with two molecules, instead of with one. The benzidine azo-dyes thus formed are termed Congo dyes, from their prototype, Congo red.

*Congo red*,  $\text{C}_6\text{H}_4 \cdot \text{N} \equiv \text{N} \cdot \text{C}_{10}\text{H}_6(\text{NH}_2) \cdot \text{SO}_3\text{Na}$ , which is made by coupling diazotised benzidine with naphthionic acid, is a scarlet powder, which dyes cotton a fast reddish brown; the free acid is blue, and the colour is thus apt to become dull on exposure to the atmosphere of towns, in which traces of sulphuric acid are usually present.

As the tetrazo-acid is a strong acid, the colour of the sodium salt is not affected by weak organic acids, nor by acid salts; Congo red paper forms therefore an excellent test for free mineral acid and for the relative strength of an organic acid (§ 116).

*Benzopurpurin*, from *tolidine* (the toluene analogue of benzidine) and naphthylamine-sulphonic acid, dyes unmordanted cotton scarlet, whilst *chrysamine*, from benzidine and sodium salicylate, is a pure yellow dye.

Bisazo-compounds of another class are obtained by coupling diazotised aminoazo-compounds with other aminic or phenolic substances; the dyes thus formed with the numerous  $\beta$ -naphthol-sulphonic acids are known as *croceins*.

*Biebrich scarlet*,  $\text{SO}_3\text{Na} \cdot \text{C}_6\text{H}_4 \cdot \text{N} \equiv \text{N} \cdot \text{C}_6\text{H}_3(\text{SO}_3\text{Na}) \cdot \text{N} \equiv \text{N} \cdot \text{C}_{10}\text{H}_6 \cdot \text{OH}$ , a crystalline powder which dyes unmordanted cotton scarlet, is thus made from diazotised aniline-azo-benzenedisulphonic acid and  $\beta$ -naphthol; the constitution of such products is determined as before by reducing them with tin and hydrochloric acid (§ 382).

**385. Synopsis.**—The azo-compounds contain in the group  $\text{N} \equiv \text{N}$ , linked to benzene or naphthalene nuclei. They are all highly coloured substances, and in combination with acid or basic groups form valuable dye-stuffs.



## SECTION XVII

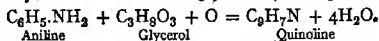
### HETERONUCLEAR COMPOUNDS

#### CHAPTER LXIX

##### PYRIDINE AND THE QUINOLINES

**386. Quinolins.**—In addition to the alkaloids of the purine group (§ 198) and the open-chain, animal alkaloids (§ 215), there are numerous vegetable bases which have well-marked physiological properties. These are the *vegetable alkaloids*; they are for the most part derived from quinoline or pyridine, basic substances to which the alkaloidal oxidation products are very closely related (Ramsay, 1878).

Quinoline is formed when quinine is distilled with potash (Gerhardt, 1842), and also occurs in coal-tar and bone-tar; it was originally obtained from the latter. It is best made synthetically, from aniline and glycerol (Skraup, 1880).



On mixing these two liquids with concentrated sulphuric acid and nitrobenzene, a vigorous action sets in, after which the mixture is boiled for some hours. The diluted product is next distilled with steam to remove any unchanged nitrobenzene, and after adding excess of caustic soda, the quinoline and excess of aniline are separated by the same process.

The distilled bases having been dissolved in dilute sulphuric acid, the solution is warmed with sodium nitrite to convert any aniline into phenol (the quinoline, being a tertiary amine, is unaffected), and on again adding excess of soda, and distilling with steam, the quinoline passes over alone.

It is extracted from the distillate with ether and redistilled (§ 249), drying being unnecessary on account of the high boiling-point. The nitrobenzene serves as an oxidising agent, and is reduced to aniline; it may be replaced by arsenic acid.

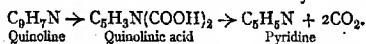
*Quinoline*,  $\text{C}_9\text{H}_7\text{N}$  (Runge, 1834), is a colourless, highly refractive liquid of aniseed odour, which boils at  $237^\circ$ , and freezes at  $-19^\circ$ ; it is slightly heavier than water, in which it

is only sparingly soluble; and has marked antiseptic properties. Quinoline is slightly alkaline to moist litmus, and is a well-defined tertiary amine.

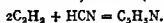
Its aminoid character is shown by its forming additive salts with acids, such as the *hydrochloride*,  $C_9H_7N, HCl$ ; and double metallic salts, such as the orange, crystalline *platinichloride*,  $(C_9H_7N, HCl)_2, PtCl_4$ ; it is a tertiary amine, for it is indifferent to nitrous acid (above), and combines additively with alkyl halides, forming ammonium compounds (§ 214), such as the *methiodide*,  $C_9H_7N, CH_3I$ , and the *benzylchloride*,  $C_9H_7N, C_6H_5Cl$ .

Quinoline is only partially resistant to oxidising agents, and when boiled with neutral permanganate solution for many hours is oxidised to quinolinic acid (§ 393), which can be extracted from the acidified product with ether.

**387. Pyridine.**—When quinolinic acid is distilled with lime, it is resolved in the normal manner into carbon dioxide and pyridine, of which it is therefore a dicarboxylic acid.



Pyridine occurs in quantity in bone-tar, from the more volatile fractions of which it is extracted by shaking with dilute acid; free ammonia is removed with acid magnesium phosphate. It is also present in coal-tar (§ 243), and may be made synthetically from acetylene and hydrogen cyanide at a dull red heat (Ramsay, 1876); its presence in the coal and bone distillates may be due to this synthesis (cf. §§ 201, 243).



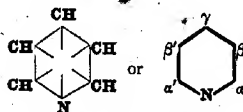
*Pyridine*,  $C_8H_5N$  (Anderson, 1849), is a colourless liquid, which boils at  $114^\circ$ , and slowly turns brown in air; its odour is rank and unpleasant. Like quinoline, it is a well-defined, tertiary amine, and forms a similar *hydrochloride*, *platinichloride* and *methiodide*; it is a stronger base, however, and dissolves in water to a feebly alkaline solution; and it is very stable towards oxidising agents.

As the nucleal constituent of many of the vegetable alkaloids, pyridine is a substance of considerable importance. Although a tertiary amine, and highly basic, it bears a striking resemblance to benzene, and yields substitutive rather than additive products. Chlorine attacks it with difficulty, and nitric acid destructively (compare § 293), but it readily yields *sulphonic acids*, which are in turn convertible into *phenols*, *nitriles* and *carboxylic acids* (§ 393), analogous to the corresponding benzene derivatives; and it forms a *hexahydro-compound* when reduced (§ 388; compare § 287).

This general analogy to benzene suggests that pyridine is a ring compound of analogous constitution, and that its molecule

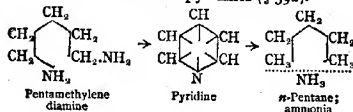


is derived from that of benzene by the substitution of a nitrogen atom for a methine group (Körner, 1869).

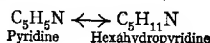


Benzenoid Structure of Pyridine.

This formula is confirmed by the reduction of the base to *n*-pentane and ammonia by hydriodic acid at 300° (Hofmann, 1883), and by a synthesis (through its hexahydro-derivative) from pentamethylene diamine (§ 388). Its validity, like that of the benzene formula, is finally established by the isomerism of the substituted pyridines (§ 392).

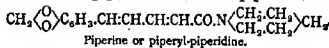


**388. Piperidine.**—When alcoholic pyridine is digested with sodium, it is reduced to hexahydropyridine (Ladenburg, 1884), from which it is recovered by oxidation with concentrated sulphuric acid at 300°.



*Hexahydropyridine* or *piperidine*,  $\text{C}_5\text{H}_{11}\text{N}$  (Cahours, 1853), which was originally obtained by the hydrolysis of piperine, the alkaloid of black pepper, is a colourless liquid, boiling at 106°; it has a pungent, ammoniacal odour, fumes with hydrochloric acid, and dissolves freely in water, forming a strongly alkaline solution.

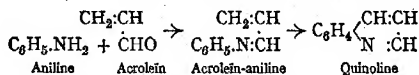
*Piperine* or *piperyl-piperidine*,  $\text{C}_{17}\text{H}_{19}\text{NO}_3$ , is a pungent, crystalline substance melting at 128°; when boiled with alcoholic potash it is hydrolysed to piperidine and piperic acid,\* from which it is reconstituted synthetically by the interaction of the acid chloride with this base (compare § 270). It is therefore the piperidine amide of piperic acid.



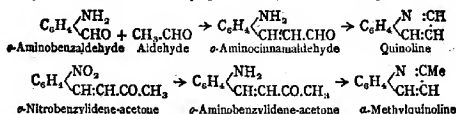
\* *Piperic acid*,  $\text{CH}_3\text{O}_2\text{C}_6\text{H}_4\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)\text{COOH}$ , which melts at 217°, is a complex derivative of cinnamic acid; when fused with potash it yields protocatechuic, oxalic and acetic acids, and the constitution thus indicated is confirmed by a synthesis from *piperonyl-acrolein*,  $\text{CH}_3\text{O}_2\text{C}_6\text{H}_4\text{CH}(\text{CH}_3)\text{CHO}$  (from piperonal, § 310, and acetaldehyde), and sodium acetate by the "cinnamic" method (§ 332).



condenses with the aniline to *acrolein-aniline* (compare § 276); and this is oxidised by the nitrobenzene, the terminal atom of the chain uniting with the benzene ring (compare § 372).

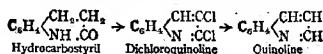


The above conclusion is confirmed by numerous other syntheses. When *o*-aminobenzaldehyde and acetaldehyde are shaken with dilute aqueous soda (§ 309), they condense to *o*-aminocinnamaldehyde,  $\text{C}_6\text{H}_4(\text{NH}_2)\text{CH:CH.CHO}$  (§ 333), which is in turn condensed to quinoline by further addition of alkali (Friedländer, 1882). *o*-Aminobenzylidene-acetone, obtained by reducing the direct nitration-product of benzylidene-acetone (§ 276), similarly condenses to  $\alpha$ -methylquinoline (Drewsen, 1883).



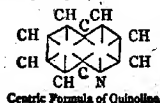
Another synthesis of quinoline is effected by means of *o*-aminohydrocinnamic acid (§ 335) which is formed by reducing the orthonitro-acid with tin and hydrochloric acid. The free acid is unknown, the substance obtained on extracting the product with ether being an internal anhydride or lactame, of the type of anthranil (§ 273).

*o*-Aminohydrocinnamic lactame or *hydrocarbostyril* is a crystalline substance, melting at  $163^\circ$ ; when warmed with phosphorus pentachloride it is converted into *dichloroquinoline*, a crystalline substance, which is reduced to the base when heated with hydriodic acid (Baeyer, 1879).



When quinoline is reduced with tin and hydrochloric acid it is converted into *tetrahydroquinoline*, an alkaline liquid which on further reduction with hydriodic acid yields a fully saturated dekahydrocompound, analogous to piperidine and hexahydrobenzene. *Dekahydroquinoline*,  $\text{C}_8\text{H}_{11}\text{N}$  (Bamberger, 1890), is a very soluble, crystalline solid, which melts at  $48^\circ$ , and resembles conine in odour (§ 396); it is a powerful base (cf. § 371).

In these reductions, as in that of  $\beta$ -naphthylamine (§ 372), the benzene ring is at first unaffected, the tetrahydro-compound is thus a secondary alicyclic amine, analogous to piperidine. By reasoning similar to that employed with the tetrahydronaphthalene derivatives, it may be inferred that the quinoline nucleus only potentially includes the benzene and pyridine nuclei, and should be represented by a single ring with ten centric bonds (Bamberger, 1890; cf. §§ 326, 356, 372).

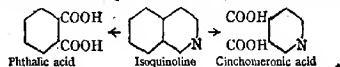


Centric Formula of Quinoline.

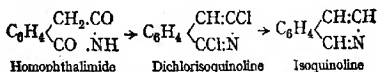
**390. Isoquinoline.**—As the nitrogen of the quinoline molecule is in the  $\alpha$ -position of the naphthalene ring (§ 372), an isomeric compound may be expected in which it occupies the  $\beta$ -position; this compound is known in isoquinoline.

*Isoquinoline*,  $C_9H_7$   $\begin{smallmatrix} \text{CH:CH} \\ \diagup \quad \diagdown \\ \text{CH:N} \end{smallmatrix}$  (Hoogewerf, 1885), is a crystalline substance, which melts at  $23^\circ$ , and boils at  $240^\circ$ ; with the exception of its behaviour on oxidation, it resembles its isomeride in almost every respect.

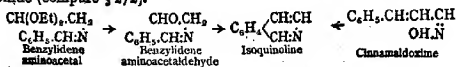
Isoquinoline is found with quinoline in coal tar, and is separated from it by fractionally crystallising the mixed sulphates; the quinoline salt is much the less soluble. Like quinoline it is oxidised by permanganate to a pyridine-dicarboxylic acid, cinchomeronic acid (§ 393), a crystalline substance isomeric with quinolinic acid; but phthalic acid is also formed, as the pyridine nucleus in isoquinoline is not quite so stable as in quinoline.



Isoquinoline is obtained synthetically when *homophthalimide*, a crystalline homologue of phthalimide (§ 324), which is made from phthalide by the cyanide synthesis (cf. § 344), is treated successively with phosphorus oxychloride and hydriodic acid.

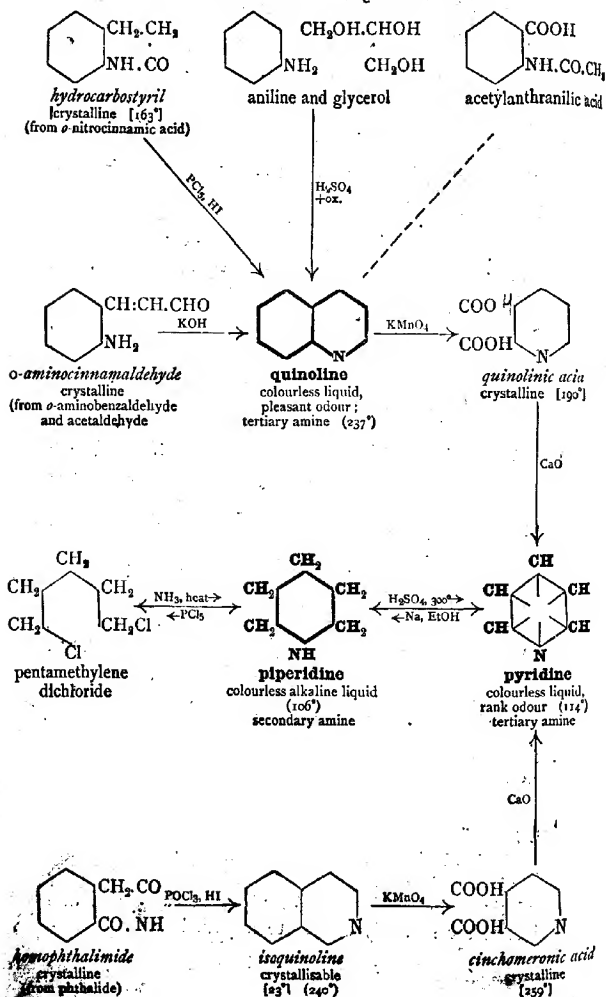


It is also produced by heating *benzylidene-aminoacetal*,  $C_6H_5.CH:N.CH_2.CH(OEt)_2$  (from benzaldehyde and aminoacetal, § 218), with concentrated sulphuric acid; and it results by a molecular transformation when *cinnamaldoxime*,  $C_6H_5.CH:CH.CH:N.OH$  (§ 332), is warmed with phosphorus pentoxide (compare § 272).



**391. Synopsis.**—Pyridine, the nuclear constituent of many of the vegetable alkaloids, is a tertiary aminoid compound, the structural formula of which is formed from that of benzene by replacing a methine group by nitrogen. Quinoline and isoquinoline are similarly related to naphthalene.

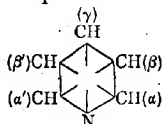
## PYRIDINE AND THE QUINOLINES.



## CHAPTER LXX

### DERIVATIVES OF PYRIDINE AND QUINOLINE

**392. The Methyl-Pyridines.**—The isomerism of the substitution products of pyridine resembles that of the benzene derivatives of the next higher order, the positions  $\alpha\alpha'$ ,  $\beta\beta'$ , and  $\gamma$  being differently situated with regard to the nitrogen atom; there are three classes of monosubstitution products and six classes of disubstitution-products.



Position Isomerism of Pyridine Derivatives

The mono-, di- and tri-methylpyridines, which are known respectively as the *picolines*, *lutidines*, and *collidines*, are liquids resembling pyridine; some of them are present in bone-tar, but they are mostly made in other ways.

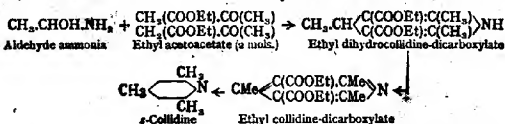
*$\alpha$ -Picoline*,  $C_6H_7N \cdot CH_3(\alpha)$ , a liquid boiling at  $129^\circ$ , is formed by heating pyridine methiodide (compare Methylaniline, § 250).  *$\beta$ -Picoline*, which boils at  $142^\circ$ , can be isolated from bone-tar, and is also formed when strychnine is distilled; it is made synthetically by dehydrating acrolein-ammonia with zinc chloride, or glycerol and acetamide with phosphorus pentoxide.  *$\gamma$ -Picoline*, a liquid boiling at  $145^\circ$ , is formed with the  $\alpha$ -compound in the isomerisation of pyridine methiodide.

*Symmetrical collidine*,  $C_8H_9N$ , a liquid which resembles pyridine, and boils at  $172^\circ$ , is readily synthesised from ethyl acetoacetate and aldehyde ammonia (Hantzsch, 1882). This synthesis, like that of quinoline from aminobenzaldehyde and acetaldehyde, is quite general; aldehyde-ammonia condenses with practically any  $\beta$ -ketonic ester, and aromatic amino-aldehydes condense with any ketonic or aldehydic compound containing the atomic grouping  $CO \cdot CH_2$ .

The above compounds condense, with evolution of heat, forming *ethyl dihydrocollidine-dicarboxylate*,  $C_8H_9N(COOEt)_2$ , a crystalline dihydro-

pyridine derivative, which is readily oxidised by nitrous anhydride in cold alcohol to the corresponding pyridine compound.

*Ethyl collidine-dicarboxylate*,  $C_8Me_3N(COOEt)_2$ , a liquid boiling at  $309^\circ$ , is convertible by the usual hydrolysis into the corresponding *potassium salt*, from which collidine is obtained by distillation with lime.

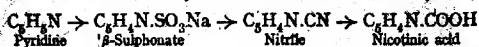


The methylpyridines resemble the methylbenzenes in their behaviour with oxidising agents, but are somewhat more resistant; they are not attacked by nitric or chromic acids, but are readily oxidised by permanganate to the corresponding pyridine-carboxylic acids, from which pyridine itself is obtained by distillation with lime.

**398. Pyridine and Piperidine Substitution Products.**—The three pyridine-monocarboxylic acids are crystalline substances, which are usually obtained as oxidation products of alkylpyridines or their derivatives; they are readily identified by their behaviour when heated. These acids resemble the aminobenzoic acids in general behaviour, and form salts both with metals and acids; they cannot of course be diazotised.

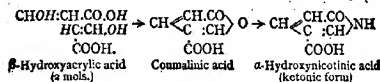
*Picolinic acid*,  $C_5H_4N.COOH(a)$ , which is formed by the oxidation of  $\alpha$ -picoline, melts at  $135^\circ$ , and then loses carbon dioxide;  $K=0.0003$ . *Nicotinic* or *pyridine- $\beta$ -carboxylic acid*, which is made by oxidising  $\beta$ -picoline and nicotine (§ 397), and also by direct synthesis from pyridine, melts at  $229^\circ$ ,  $K=0.0014$ . *Isonicotinic acid*,  $C_5H_4N.COOH(\gamma)$ , which is formed by oxidising  $\gamma$ -picoline, sublimates when heated under ordinary pressure, but melts at  $309^\circ$  when heated in a closed tube;  $K=0.0011$ .

The synthesis of nicotinic acid from pyridine is exactly parallel to that of benzoic acid from benzene. When pyridine is heated with concentrated sulphuric acid, it is sulphonated to *pyridine- $\beta$ -sulphonic acid*, the sodium salt of which is converted into the corresponding  *$\beta$ -cyanopyridine* by distillation with potassium cyanide. This cyano-compound is identical with *nicotinonitrile*, and yields nicotinic acid when hydrolysed.



*$\alpha$ -Hydroxynicotinic acid* is formed by the action of ammonia, at the ordinary temperature, on *coumalinic acid*,  $C_5H_5O_3.COOH$ , a lactonic acid (§ 356), which is obtained by the action of concentrated sulphuric acid on *maleic acid*; an oxidation product,  *$\beta$ -hydroxyacrylic acid*, intervenes. The

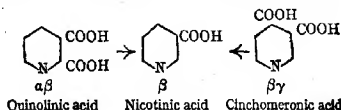
synthesis is of interest, as indicating the lines on which pyridine compounds may be formed naturally in the living plant-cell (compare also § 407).



The six pyridine-dicarboxylic acids, the isomerism of which resembles that of the bromoxylenes, are crystalline substances resembling the monocarboxylic acids, into which they are converted by distillation with a single equivalent of lime.

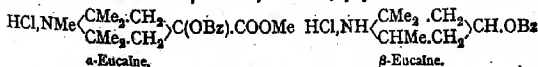
*Quinolinic* or *pyridine- $\alpha\beta$ -dicarboxylic acid*, is a crystalline substance melting at  $190^\circ$ ,  $K=0.3$ ; *cinchomeronic acid*, the corresponding  $\beta\gamma$  acid, melts at  $250^\circ$ ,  $K=0.21$ .

The orientation of these acids follows from their formation from quinoline and isoquinoline, whilst that of the monocarboxylic acids (and connected mono-substitution products) is deduced from the genetic relations of the two sets of acids. The juxtaposition of the carboxyl groups is also shown by their conversion into anhydrides by acetic anhydride (cf. § 342).



By distilling the dicarboxylic acids with a single equivalent of lime, or even by heating them alone, they are converted into the monocarboxylic acids, in the same way as phthalic acid into benzoic acid. Quinolinic acid yields only nicotinic acid, whilst cinchomeronic acid yields both nicotinic and isonicotinic acids. The nicotinic carboxyl is thus common to both dicarboxylic acids, or in the  $\beta$ -position; the isonicotinic carboxyl is therefore in the  $\gamma$ -position, and that of picolinic acid in the  $\alpha$ -position.

The synthetic drug  *$\alpha$ -eucaine*, the aqueous solution of which is employed as a local anaesthetic in place of cocaine (§ 398) is derived from *piperidine- $\gamma$ -carboxylic (hexahydroiso-nicotinic) acid*. The related drug,  *$\beta$ -eucaine*, which has very similar properties, and is much more easily prepared, is the *hydrochloride* or *lactate* of  *$\gamma$ -benzoxy-trimethylpiperidine*.



The eucaine bases are made synthetically from acetone. When acetone is saturated with gaseous ammonia, it is slowly converted into *diacetoneamine*, a soluble, ammoniacal liquid, which may also be prepared by the

M M

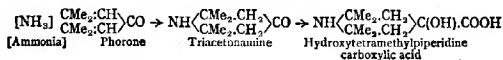


direct action of ammonia on mesityl oxide (§ 107). This base condenses with aldehyde (i.e. the sparingly soluble *acid oxalate* with alcoholic par aldehyde) forming  $\gamma$ -ketotrimethylpiperidine, a deliquescent, crystallisable basic substance, which yields the corresponding secondary alcohol when reduced with sodium amalgam.

$\gamma$ -Hydroxytrimethylpiperidine is a basic substance which is resolvable into two stereoisomeric forms (§ 326); the *trans*-modification is a stable, crystalline substance, the benzoate of which is the base of  $\beta$ -eucaine,



$\alpha$ -Eucaine is obtained by a somewhat more complicated process from triacetanamine or ketotetramethylpiperidine, a crystalline, basic substance, which is made by digesting phorone (§ 107) with aqueous ammonia. This is converted by the cyanhydrin synthesis (compare § 165) into a hydroxy-carboxylic acid, the methyl ester of which is converted into the eucaine base by successive methylation and benzylation.



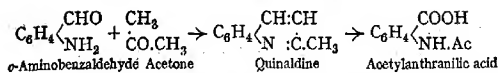
Many other substitution products of pyridine have been prepared, such as the chloropyridines, and the hydroxy-pyridines or pyridine-phenols.  $\beta$ -Hydroxypyridine,  $\text{C}_5\text{H}_4\text{N} \cdot \text{OH}$ , is a crystalline, phenolic substance, which is formed from the sodium  $\beta$ -sulphonate, in the same way as phenol from the benzene-sulphonate.

Pyridine cannot be nitrated, and the aminopyridines have therefore to be made indirectly (§ 397). Dihydroxypyridine, however, is directly convertible into a nitro-compound resembling the nitrophenols; the corresponding trihydroxy-compound is a powerful reducing agent (cf. § 305).

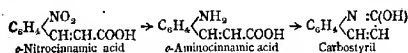
**394. Derivatives and Analogues of Quinoline.**—Quinoline can be chlorinated, sulphonated and nitrated, and on account of the complete asymmetry of its molecule, the isomerism of its substitution products is very complex; there are no fewer than seven mono-substitution products of each kind.

*Cinchoninic* or *quinoline- $\gamma$ -carboxylic acid* (§ 400) is a crystalline substance, which is formed by the oxidation of cinchonine, and is resolved into carbon dioxide and quinoline by distillation with lime.

Some of the methyl quinolines can be formed synthetically. *Quinaldine* or  *$\alpha$ -methylquinoline*, a liquid resembling quinoline, and boiling at  $246^\circ$ , is formed by condensing *o*-aminobenzaldehyde with acetone (compare § 389). When oxidised with permanganate it yields quinoline-carboxylic acid, whilst with dilute nitric acid acetaminobenzoic acid is formed (§ 389).



Other quinoline substitution products can also be formed synthetically. *Carbostyryl* or *o-hydroxyquinoline*, a white crystalline substance melting at 199°, is formed by reducing *o*-nitrocinnamic acid (§ 333) with tin and hydrochloric acid; the amino-group of the *aminocinnamic acid* at once condenses with its carboxyl.



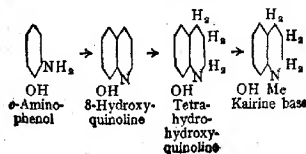
The glycerol synthesis is very generally applicable, and most ring amino-compounds, provided that an ortho-position to the amino-group is unoccupied, condense in the same way as aniline. Naphthylamine and anthraniline thus form with glycerol naphthoquinoline and anthraquinoline, which are analogous to quinoline in their actions.

The first substance prepared in this way was the dye *alizarin blue*, (*dihydroxy-anthraquinolinequinone*), from amino-alizarin (Prud'homme, 1877); it was the close resemblance of this compound to quinoline derivatives which suggested the quinoline synthesis.

The *naphthoquinolines*,  $\text{C}_{13}\text{H}_9\text{N}$ , are crystalline substances, which bear exactly the same relation to phenanthrene as quinoline to naphthalene; one of the methine groups of a terminal ring is replaced by a tertiary nitrogen atom. They form *tetrahydro-compounds* analogous to the naphthylamines, and *ar-* and *ac-octahydro-compounds* analogous to the reduced naphthylamines (§ 372).

The antipyretic, *kairine* (O. Fischer, 1883), a crystalline phenolic derivative of tetrahydroquinoline (§ 389), is made by direct synthesis, and affords an excellent example of the numerous applications of the glycerol-aniline method.

The *hydroxyquinoline* obtained from *o*-hydroxyaniline (*o*-aminophenol, § 294) is reduced to the corresponding *tetrahydro-compound*, the tertiary amino-group thus becoming secondary (§ 388); this secondary amine is then heated with methyl iodide, yielding a tertiary amine, *N-methyl-tetrahydrohydroxyquinoline*, of which *kairine* is the *hydrochloride*.



Many ring compounds have been synthesised analogous to quinoline and pyridine, and others have also been made, in which two or more of the methine groups of benzene or naphthalene are replaced by nitrogen.

*Acridine*,  $C_6H_4 \begin{smallmatrix} CH \\ N \end{smallmatrix} C_6H_4$ , a chromogenic base, which is present in

crude anthracene, and *phenanthridine*,  $\begin{smallmatrix} C_6H_4 \cdot CH \\ C_6H_4 \cdot N \end{smallmatrix}$  bear a relation to anthracene and phenanthrene somewhat similar to that of quinoline to naphthalene (compare Naphthoquinoline, above). Acridine yields *acridinic* or *quinoline- $\alpha\beta$ -dicarboxylic acid* when oxidised, and is made synthetically by dehydrating *formodiphenylamide*,  $H \cdot CO \cdot NPh_2$  (from diphenylamine and formic acid), with zinc chloride.

*Piperazine*,  $NH \begin{smallmatrix} CH_2 \cdot CH_2 \\ CH_2 \cdot CH_2 \end{smallmatrix} NH$ , is formed by the interaction of ethylene dibromide and ethylene diamine; the related ditertiary amine, *pyrazine*,  $N \begin{smallmatrix} CH - CH \\ CH = CH \end{smallmatrix} N$ , is a similar crystalline compound.

**395. Synopsis.**—Pyridine and quinoline form substitution products, alkyl derivatives, and reduction products, which resemble those of benzene and naphthalene in constitution, but owing to the presence of the nitrogen differ from them in isomerism and general properties.

## CHAPTER LXXI

### THE VEGETABLE ALKALOIDS: CONINE AND THE TROPINE AND CINCHONA GROUPS

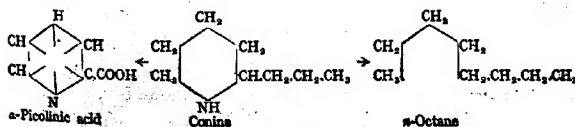
**396. Conine.**—Most of the vegetable alkaloids are derived from pyridine or analogous cycloid bases; some are free from oxygen, and these are usually liquid, but the majority of them contain this element. One of the simplest of the volatile, non-oxygenated alkaloids is conine, the poison of hemlock.

The alkaloid is present as a salt of *caffete* (*dihydroxycinnamic*) acid, and is obtained by distilling the seed with potash. The yield is improved by extracting the seed with dilute acetic acid, and decomposing the solution of the acetate with magnesia; the base is then extracted with ether, and purified by distillation under reduced pressure.

*Conine* or *d-α-propylpiperidine*,  $C_8H_{15}N$ ,  $CH_3 \cdot CH_2 \cdot CH_2 \cdot$  (Giesecke, 1827), is a light, colourless, soluble oil, of rank and penetrating odour; it boils at  $167^\circ$ , freezes at  $-3^\circ$ , and is dextrogyrate,  $[\alpha]_D = +15^\circ$ . It is a secondary amine, resembling piperidine, and a strong base, its solution being alkaline.

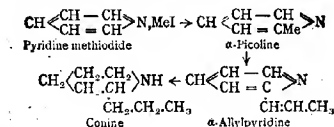
It forms a crystalline, additive *hydrochloride* and *platinichloride*, and, as a secondary amine, a yellow oily *nitroso-compound*, and a tertiary *methyl derivative*. Like piperidine it is reduced by hydriodic acid to ammonia and a normal paraffin, *n*-octane.

When conine is boiled with aqueous permanganate it is oxidised to picolinic acid (§ 393); and this, coupled with its general resemblance to piperidine, and the fact that it yields *n*-octane when destructively reduced, indicates that it is *α*-propylpiperidine. The correctness of the inference is proved by synthesis (Ladenburg, 1886)—the first synthesis of a natural alkaloid.



When the  $\alpha$ -picoline, which is formed by the isomerisation of pyridine methiodide (§ 392), is heated with paraldehyde at  $260^\circ$ , it condenses to  $\alpha$ -allylpyridine, a liquid which resembles the alkyl-pyridines; and on boiling this base with sodium in alcohol it is reduced to  $\alpha$ -propylpiperidine, which is identical with *inactive conine*.

Synthetic  $\alpha$ -propylpiperidine, like all synthetic compounds (§ 141), is optically inactive, but on fractionally crystallising its acid tartrate, the less soluble crystals consist of *d-conine hydrogen tartrate*, and on distillation with potash yield *d-conine*, identical with the natural base.

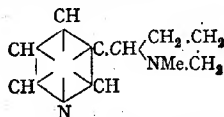


**397. Nicotine.**—The volatile alkaloid nicotine is obtained by distilling with lime the aqueous infusion of tobacco leaves, in which the base is present as the *malate*.

Nicotine is also formed by distilling tobacco alone, and thus accumulates in an impure form in the stems of tobacco pipes; good tobacco contains less nicotine than the commoner varieties. It is purified by conversion into its crystalline hydrochloride, from which it is liberated by concentrated soda; it is then extracted with ether, and fractionated under low pressure, in an atmosphere of hydrogen.

*Nicotine* or *1-pyridyl-methylpyrrolidine*,  $\text{C}_8\text{H}_{14}\text{N}_2\cdot\text{NMe}$  (Posselt, 1828), is a colourless liquid of very rank and unpleasant odour; it boils at  $247^\circ$ , and is strongly laevogyrate,  $[\alpha]_D = -162^\circ$ . Although it resembles conine in odour, and in its instability in air, it is a ditertiary base, and is akin to pyridine rather than piperidine in its chemical actions.

A study of its oxidation products leads to the conclusion that it is the  $\beta$ -pyridyl derivative of a saturated cycloid base, *N*-methylpyrrolidine (§ 407), and the correctness of this inference is again verified by synthesis (Pictet, 1903).

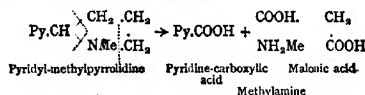


Nicotine as Pyridylmethylpyrrolidine.

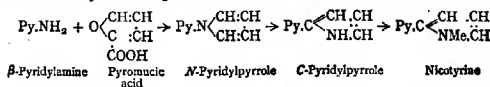
Nicotine is oxidised by chromic acid to nicotinic acid (§ 393), whilst by the gentler oxidising action of aqueous bromine and baryta, methylamine and malonic acid are also obtained. On reduction with sodium in alcohol it yields a *hexahydro-compound*, which is now completely saturated.

These results are embodied by the rational formula  $\text{C}_8\text{H}_{14}\text{N}_2\cdot\text{NMe}$ , which represents nicotine as a pyridyl derivative of a saturated tertiary

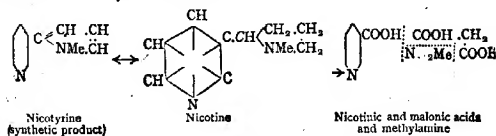
amine,  $C_4H_9NMe$ . This compound, from its composition, is necessarily cycloid in constitution; and the oxidation to methylamine and malonic acid (the fourth carbon atom remaining attached to the pyridine ring) suggests the presence of a five-membered or pyrrolidine ring (§ 407) analogous to that of methylpiperidine (§ 388). This is confirmed by synthesis. The pyridyl nucleus is necessarily next the methylimino-group, or malonic acid could not be formed.



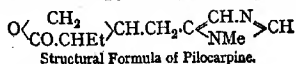
$\beta$ -Aminopyridine, which is made by the action of alkaline hypobromite on nicotinamide (cf. § 212), condenses with pyromucic acid (§ 406), forming *N*-pyridyl-pyrrole (cf. § 407), a basic liquid, which is transformed by heat into the isomeric *C*-pyridyl-pyrrole (cf.  $\alpha$ -Picoline, § 392). This last compound is converted by methylation (see Phthalimide, § 324) into *C*-pyridyl-*N*-methylpyrrole, which is identical with *nicotyrine*, a basic liquid formed by oxidising nicotine with moist silver oxide.



By alternate treatment with halogens and reducing agents, *nicotyrine* is reduced to *racemic nicotine*, the *lævo*-constituent of which, isolated in the same way as *d*-conine, is identical with natural nicotine (Pictet, 1903). *Nicotyrine* and the pyridyl-pyrroles give the characteristic pyrrole colours with pine-wood and hydrochloric acid (§ 407), but nicotine, being a reduced pyrrole derivative, does not do so.



*Pilocarpine*,  $C_{11}H_{16}N_2O_2$ , a strongly dextrogyrate, liquid alkaloid obtained from jaborandi, and its crystalline stereoisomeride, *pilocarpidine*, into which it is converted by distillation, are lactonic derivatives of methylglyoxaline (§ 408), a base allied to pyrrole (Jowett, 1902).

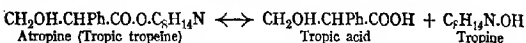


**298. The Tropane Alkaloids : Cocaine.**—The crystalline alkaloids fall naturally into several distinct classes, according to their origin and derivation. Atropine, hyoscyamine and cocaine, are

derived from tropine, a somewhat complex derivative of pyrrolidine, piperidine, and cycloheptane.

Atropine, the poison of the deadly nightshade, is not present as such in the plant, but is formed by the action of acids or alkalies on a stereo-isomeric alkaloid, *hyoscyamine* (compare Tropine, below); the expressed juice is simply made alkaline with potash, and the crude atropine extracted with ether and purified by crystallising its sulphate.

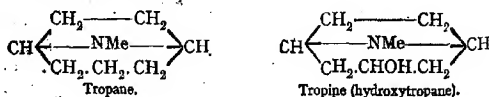
*Atropine*,  $C_{17}H_{23}NO_3$  (Geiger, 1830) is a crystalline, optically inactive, poisonous base. It is hydrolysed by baryta water to *i-tropic* ( $\alpha$ -phenylhydracrylic) acid, and a simpler base, tropine (below), and is reproduced from these components by heating with dilute hydrochloric acid; it is therefore *tropine i-tropate*, and is termed a *tropeine* (Ladenburg, 1879).



Analogous tropeines can be made similarly from tropine with other acids; *homatropine*, which is the next homologue of atropine, and closely resembles it in properties, although not nearly as poisonous, is *phenylglycollic tropeine*; both compounds are used in ophthalmic surgery.

*Tropine*,  $C_8H_{15}NO$ , which is a crystalline, optically active substance melting at  $62^\circ$ , is a saturated tertiary amine; it is also a secondary alcohol, for it is converted by gentle oxidation into *tropinone*,  $C_8H_{13}NO$ , a ketonic compound from which it is recoverable by the usual reduction. Tropinone is further reducible to a cycloid amine, *tropane*,  $C_8H_{15}N$ ; it is therefore *ketotropane*, and tropine is *hydroxytropane* or *tropanol*.

A study of the chemical relations of tropinone leads to the conclusion that tropane is a saturated, bridged-ring compound (§ 342) derived from cycloheptane (cf. § 288), the bridge consisting of a methylimino-group,

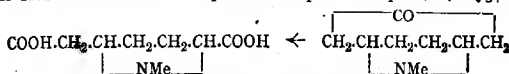


*Tropinone*,  $\text{CO}(\text{CH}_2)_2\text{C}_4\text{H}_9\text{NMe}$ , is a volatile, crystalline, optically inactive substance, melting at  $42^\circ$ . It is a saturated tertiary amine, and as it forms a *dibenzylidene derivative*, its molecule contains the group  $\text{CH}_2\text{CO}.\text{CH}_2$  (§ 341). *Tropane*,  $\text{CH}_2(\text{CH}_2)_2\text{C}_4\text{H}_9\text{NMe}$ , which is a basic liquid boiling at  $167^\circ$ , is obtained by reducing tropinone with zinc and hydriodic acid; when further oxidised, it is converted into a racemic dibasic acid, *i-tropic acid*,  $\text{COOH}.\text{CH}:(\text{COOH})\text{C}_4\text{H}_9\text{NMe}$ .

All these compounds, like tropine, form additive *methiodides*, and are therefore tertiary amines, but unlike pyridine they are not reducible by

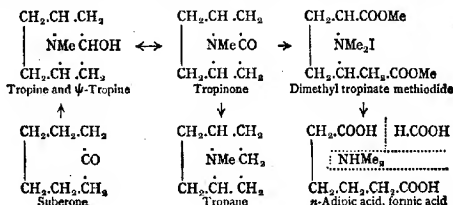
sodium in amyl alcohol (§ 388), and hence are saturated (tropine is converted into a stereoisomeride, *ψ-tropine*). The clue to their inner constitution is obtained by the formation of dimethylamine, formic acid and *n*-adipic acid, when *dimethyl tropinate methiodide* is fused with potash; this shows that the tropinic acid molecule contains an NMe-group (the methiodide of which gives the dimethylamine), associated with a normal six-carbon chain.

If this group and chain form an *N*-methylpyrrolidine ring (§ 397) as below, both the stability and optical asymmetry of tropinic acid, and the saturated character of tropane and tropine are explained (cf. § 342).



Tropinic Acid and Troponone as Derivatives of *N*-Methylpyrrolidine.

These formulæ also show that tropine and its congeners are derived from *N*-methylpyrrolidine and cycloheptane, as well as from *N*-methylpyrrolidine; they have been confirmed by the synthesis of tropine from *suberone*, the cycloid ketone (§ 287) of suberic acid (Willstätter, 1901).



The well-known drug, cocaine, is found in coca leaves, and after precipitating tannin, etc., with basic lead acetate is extracted from their alkaline infusion with ether.

*l*-Cocaine,  $\text{C}_{17}\text{H}_{21}\text{NO}_4$  (Niemann, 1860), which is a *l*-avo-gyrate, crystalline substance, melting at  $98^\circ$ , has marked basic properties and forms well-defined crystalline salts.

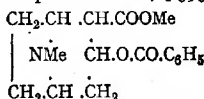
It is hydrolysed by alkalis to methyl alcohol and *benzoyl-ecgonine*, a crystalline amino-acid, of which it is thus the *methyl ester*; and *benzoyl-ecgonine* is further hydrolysable to benzoic acid and an alcoholic amino-compound, *ecgonine*, of which it is thus the *benzoyl-derivative*.

Cocaine can be reconstituted from *l*-ecgonine by benzylation and methylation, and is manufactured in this manner, as several similar alkaloids of little therapeutical value yield *l*-ecgonine when hydrolysed. *Cocaine hydrochloride* is used in dental and ophthalmic surgery for deadening pain, as it has the power of paralyzing superficial nerves; it has the same effect on the coats of the stomach, and is sometimes used to deaden hunger; but it is an active poison.



1-Ecgonine,  $C_8H_{15}NO.COOH$ , which is a very soluble, crystalline substance, melting at  $205^\circ$ , is *tropine-carboxylic acid*; it yields tropinone when gently oxidised, and its *racemic modification* is formed synthetically by reducing the unsaturated acid obtained by the action of carbon dioxide on *sodium tropinone* (compare §§ 308, 107—Sodium Acetone).

The *racemic cocaine* made from synthetic ecgonine (Willstätter, 1901) is identical with the natural alkaloid, except in optical activity, and cocaine is therefore *methyl lævobenzoyl-tropine-carboxylate* (compare Eucaine, § 393).



Structural Formula of Cocaine.

**399. The Cinchona Alkaloids.**—Perhaps the most important of the vegetable alkaloids is quinine, which, together with cinchonine and other related bases, such as quinidine and cinchonidine, is found in cinchona bark, combined with tannin and quinic acid (§ 311).

The associated alkaloids are extracted from the finely-divided bark with dilute sulphuric acid, and precipitated with soda; the mixture of sulphates, obtained by neutralising the alcoholic solution with dilute sulphuric acid, being fractionally crystallised from water. Quinine sulphate is the least soluble, and therefore crystallises first, whilst cinchonine sulphate is next in order, and separates from the mother-liquor; the bases are then precipitated from the sulphates by ammonia, and crystallised from alcohol.

*Quinine*,  $C_{20}H_{24}N_2O_2$  (Pelletier, 1820), forms colourless, silky crystals, and melts when anhydrous at  $173^\circ$ ; it is strongly lævogyrate,  $[\alpha]_D = -164^\circ$ . The base is insoluble in water, but soluble in alcohol, ether and dilute acids, forming intensely bitter solutions; dilute solutions of the *sulphate* show a fine blue fluorescence. The sulphate and *monohydrochloride* are used medicinally as antipyretics.

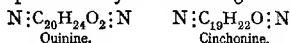
Quinine is readily identified by means of the coloured oxidation products, which it yields with chlorine and ammonia; with chlorine or bromine water followed by ammonia, a green precipitate is formed, which dissolves in excess of ammonia to a clear, dark-green solution, whilst if potassium ferrocyanide is added before the ammonia, but after the halogen, a crimson coloration is obtained.

*Cinchonine*,  $C_{19}H_{22}N_2O$  (Pelletier, 1820), which is a silky, crystalline substance melting at  $250^\circ$ , is less bitter than quinine, and of little value medicinally. It is strongly dextrogyrate,  $[\alpha]_D = +234^\circ$ ; its *sulphate* is not fluorescent, and it does not give colour reactions with chlorine.

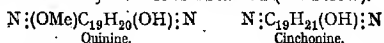
The only characteristic salt of cinchonine is the *ferrocyanide*, which is very sparingly soluble, and is hence precipitated in small crystals on adding potassium ferrocyanide to a strong solution of the alkaloid; cinchonine may be detected, however, in the absence of better characterised bases, by means of the general alkaloid tests.

All alkaloids, and most aminoid compounds, are characterised by forming certain insoluble compounds, from which they are set free by caustic or carbonated alkalies. The *phosphomolybdates* are buff or yellowish powders, which are precipitated by adding sodium phosphomolybdate to the neutral solutions; the *mercuriodides* are similarly precipitated, by a solution of mercuric iodide in potassium iodide; and brown *periodides* are precipitated by a solution of iodine in potassium iodide. The mercuriodide test (Mayer) is very sensitive.

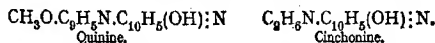
**400. Constitution of Quinine and Cinchonine.**—As quinine forms two classes of salts, it is a di-acid base, and as these salts are additive, and it forms a *platinichloride* containing a single equivalent of the base (§ 59), it is a diamine; further, as it is converted successively into a *methiodide* and *dimethiodide* when heated with methyl iodide, it is a tertiary diamine. The same applies to cinchonine, and the two alkaloids are therefore represented by the following formulæ.



Both quinine and cinchonine yield crystalline *monacetyl derivatives* when boiled with acetic anhydride, so that their molecules contain alkylic hydroxyl, and the quinine molecule contains in addition a methoxyl group, for when the base is boiled with concentrated hydriodic acid, a single equivalent of methyl iodide is obtained (see below).



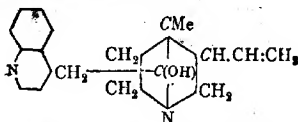
As cinchonine yields quinoline when distilled with lime, and quinine under the same conditions yields *methoxyquinoline*, the above results may be summarised in the following partial formulæ.



The second main group is linked with the  $\gamma$ -carbon of the quinoline molecule, for on oxidising cinchonine and quinine with nitric acid, *cinchoninic* or *quinoline- $\gamma$ -carboxylic acid* (§ 394), and the corresponding *methoxy-acid*, are formed; the  $\gamma$ -position of the carboxyl in both these acids follows from their convertibility into cinchomeronic acid (§ 393).

This second group is probably constituted somewhat simi-

larly to tropine, and cinchonine may be provisionally represented by the following formula.



Probable Structural Formula of Cinchonine.

(The quinine molecule contains in addition a methoxyl-group in the quinoline benzene nucleus.)

Phenolic methoxyl groups are hydrolysed quantitatively by boiling hydriodic acid, and as the resulting methyl iodide is in turn converted quantitatively into silver iodide by alcoholic silver nitrate, the percentage of methoxyl in the substance, and thus the number of methoxyl groups in the molecule is readily determined (Zeisel, 1886).



In the simplest modification of this process (Perkin, *sen.*, 1903), the substance is boiled gently with distilled hydriodic acid (b. p. 126°) in a long-necked distilling-flask, through which a stream of carbon dioxide is passed throughout the operation. The flask is heated in a glycerine bath, and the delivery tube is tilted upwards, to serve as a reflux condenser for the small amount of steam which escapes from the boiling acid.

The methyl iodide vapour, which is carried on by the carbon dioxide is collected in a Volhard trap (§ 114), containing a strong solution of silver nitrate in somewhat diluted alcohol; and the precipitated silver iodide is collected and weighed.

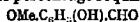
When vanillin (§ 310) was treated in this manner, the following result was obtained.

0.309 gram vanillin gave 0.309 gram AgI.

The percentage of methoxyl, one methoxyl group ( $=31$ ) being eliminated for each molecule of silver iodide ( $=235$ ), was therefore

$$\frac{0.309 \times 31 \times 100}{235 \times 0.309} = 20.4,$$

which agrees exactly with the percentage required by the formula



**401. Synopsis.**—The vegetable alkaloids, such as conine and quinine, are complex aminoid compounds derived from pyridine and allied cycloid bases. Those which do not contain oxygen are usually liquid, whilst the others are colourless, crystalline solids.



## CHAPTER LXXII

### THE VEGETABLE ALKALOIDS: NUX VOMICA AND OPIUM

**402. The Nux Vomica Alkaloids.**—The poisonous character of the nux vomica bean is due to the presence of two quinoline alkaloids, strychnine and brucine, which may be extracted by boiling the powdered beans with dilute alcohol.

The accompanying tannin having been precipitated with lead acetate, the mixed bases are precipitated with magnesia, and fractionally crystallised from alcohol; the strychnine, which is much the less soluble, separates first, whilst the brucine remains in the mother liquor.

The brucine mother-liquor is evaporated to dryness with acetic acid (the strychnine acetate being thus dissociated); on extracting the residue with water the brucine salt alone dissolves, and the base is precipitated with ammonia.

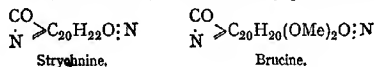
*Strychnine*,  $C_{21}H_{22}N_2O_2$  (Pelletier, 1810), is a laevogyrate, crystalline substance, melting at  $268^\circ$ ; its solutions are extremely bitter, but in very dilute form are used as tonics. *Brucine*,  $C_{21}H_{20}(OMe)_2N_2O_2 + 4H_2O$  (Pelletier, 1812), is also laevogyrate, and melts when anhydrous at  $178^\circ$ . Both alkaloids are characterised by brilliant colour reactions.

When a fragment of a strychnine salt is dissolved in a few drops of concentrated sulphuric acid (warmed, if necessary), and a crystal of potassium dichromate is drawn through the cold solution, a dark violet oxidation product is formed, which gradually changes to red and yellow.

Similarly brucine is converted by concentrated nitric acid into an orange-red colouring matter, which is changed to violet by cold stannous chloride, provided that nitrous acid has previously been expelled by boiling.

Strychnine and brucine are tertiary monamines<sup>2</sup>, as they form only one class of salt, and combine additively with a single equivalent of methyl iodide; the second nitrogen atoms are not in aminoid combination, but are probably present in lactimino-form (§ 338). Brucine is a dimethoxy-compound (§ 400), and when fused with potash yields methylpyridines and tetrahydroquinoline; strychnine is oxidised by nitric acid to picric acid, and a derivative of dihydroquinoline.

Beyond the fact that they are both tertiary quinoline derivatives little is yet known of their inner constitution, and they can only be represented by the following partial formulæ.



The extremely toxic character of these and other alkaloids often renders their detection necessary in presence of relatively large quantities of foreign organic matter, such as the contents of a stomach. For this purpose a method has been devised (Stas, 1852) which is applicable to practically all alkaloids.

The mass is acidified with tartaric acid and strained, and the fluid shaken with ether to dissolve out fat, and other objectionable matter. The acid solution is then made alkaline with sodium carbonate, and the liberated alkaloid extracted with ether-chloroform or amyl alcohol.

The filtered extract is evaporated at a low temperature, and examined, first by the general tests (§ 399), and then, if an alkaloid be present, by special tests such as the above; any ptomaines (§ 215) which may have been formed by the decomposition of the proteid matter, will of course be found in the final product.

**403. The Opium Alkaloids: Morphine and Codeine.**—The narcotic properties of opium, the dried sap of green poppy capsules, are mainly due to morphine, which is associated with other alkaloids, such as codeine, papaverine, and narcotine.

The morphine in opium preparations, such as laudanum, is always associated with *meconic acid*, a pyrone derivative (§ 409) which is recognised by the intense, purple-red colour of its ferric compound, even in presence of dilute hydrochloric acid.

To isolate the alkaloid, opium infusion is boiled with milk of lime, in which the morphine alone is soluble, and the filtered solution is saturated with ammonium chloride; the lime is thus converted into calcium chloride, and the morphine, deprived of its solvent, is slowly precipitated. The dry precipitate is recrystallised from amyl alcohol.

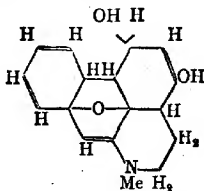
*Morphine*,  $\text{C}_{17}\text{H}_{19}\text{NO}_3$  (Sertürner, 1817), is a crystalline, strongly laevogyrate base, which is much less bitter than most of the alkaloids. The silky crystalline *hydrochloride* is used in medicine; when injected beneath the skin in small doses it acts as a stimulant, whilst in somewhat larger doses it is narcotic; in still larger amounts it is poisonous.

Morphine differs markedly from the other common alkaloids. It is a tertiary monamine, but although alkaline in alcoholic solution, it is soluble in caustic alkalis, like the aminophenols; and the phenolic character thus indicated is borne out by its

conversion into a blue *ferric compound*, and into a *methoxy-compound* by interaction with methyl iodide in alkaline solution.

Like the aminophenols also, it is very readily oxidised, and thus reduces cold silver solutions, and liberates iodine from iodic acid; its benzenoid relation is further evidenced by its oxidation to picric acid by nitric acid, and to protocatechuic acid by fusion with potash.

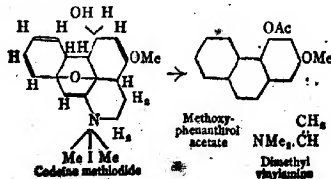
Morphine is derived from a *trihydroxy-tetrahydrophenanthramine*,  $\text{NH}_2 \cdot \text{C}_{14}\text{H}_{10}(\text{OH})_3$  (Knorr, 1899 et seq.), and is probably represented by the following structural formula; codeine being the corresponding phenolic methyl ether. A synthetic naphthalene derivative of analogous constitution has been made, having very similar properties (compare Tetrahydro- $\beta$ -naphthylamine, §§ 371, 372).



Probable Structural Formula of Morphine.

The alkaloid forms an additive *methiodide*, and as it yields a *diacetyl compound*, and under special conditions a *triacyl compound*, two of the oxygen atoms are hydroxylic, whilst the third is probably ethereal. The second hydroxyl group is alcoholic, for the methoxy-compound, codeine, is no longer phenolic in character.

The clue to its inner constitution is given by the large yield of phenanthrene (§ 378), which is obtained when it is distilled with zinc-dust. The relation to this hydrocarbon is established by the conversion of methyl-morphine (codeine) methiodide into *methoxyphenanthrol acetate*,  $\text{OMe} \cdot \text{C}_{14}\text{H}_9 \cdot \text{OAc}$ , and *dimethylvinylamine*,  $\text{CH}_2\text{:CH} \cdot \text{NMe}_2$ , when it is heated successively with potash and acetic anhydride; and is confirmed by many similar resolutions.

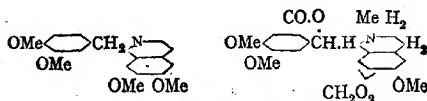


*Codeine* or *methylmorphine*,  $\text{OMe} \cdot \text{C}_{17}\text{H}_{17}\text{NO} \cdot \text{OH}$ , which is made by methylating morphine in alkaline solution, is a crystalline substance melting at  $150^\circ$ ; it occurs naturally in opium, and may be extracted from the lime precipitate obtained in the isolation of morphine. Physiologically it is much less active, and chemically much more stable.

The increased stability is due to the protection of the phenolic group. Codeine is insoluble in alkalis, indifferent to ferric chloride, and has little or no reducing power; and when boiled with hydriodic acid it is reconverted into morphine. *Heroine* or *diacetylmorphine*,  $\text{C}_{17}\text{H}_{17}\text{NO}(\text{OAc})_2$ , on the other hand resembles morphine physiologically, and is less stable than codeine, owing to the easy hydrolysis of the acetyl groups.

**404. The Opium Alkaloids: Papaverine and Narcotine.**—The constitution of papaverine and narcotine has also been fully investigated, with the result of proving these alkaloids to be isoquinoline derivatives.

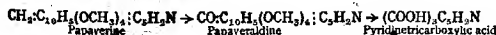
*Papaverine*,  $\text{C}_{20}\text{H}_{21}\text{NO}_4$  (Merck, 1848), is a crystalline substance melting at  $147^\circ$ , which occurs with narcotine in the lime precipitate. Its constitution as *dimethoxybenzyl-dimethoxyisoquinoline* is represented by the following formula (Goldschmidt, 1888). *Narcotine*,  $\text{C}_{23}\text{H}_{23}\text{NO}_7$ , which melts at  $176^\circ$ , is very similarly constituted, the nucleus being identical.



Structural Formulae of Papaverine and Narcotine.

Papaverine is a tertiary monamine; it forms only one class of salts, and combines additively with one equivalent of methyl iodide; and as its molecule contains four methoxyl groups (§ 400), its formula may be written provisionally as  $\text{C}_{16}\text{H}_9(\text{OCH}_3)_4:\text{N}$ .

When cautiously oxidised with aqueous permanganate, it is converted into a lactonic compound, *papaveraldine*, which shows that its molecule contains a methylene group in a position favourable to oxidation (§ 354); by the further action of the same agent, various degradation products are obtained, the most important of which are *dimethoxyphthalic acid* and *pyridine- $\alpha\beta\gamma$ -tricarboxylic acid*.

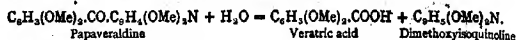


When fused with potash, papaveraldine is resolved hydrolytically into veratric (dimethylprotocatechuic) acid (cf. § 310) and *dimethoxyisoquinoline*, so that its molecule contains the nuclei of these compounds. This leads directly to the conclusion that it is a tetramethyl derivative of benzyloquinoline, in the molecule of which (as it yields pyridine- $\alpha\beta\gamma$ -tricarboxylic

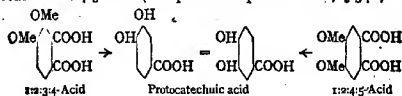
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acid when further oxidised) the benzyl group is linked to the carbon atom, between the nitrogen and the benzene ring (see above).

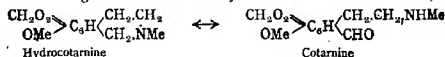


The position of the methoxyl groups in the isoquinoline part of the molecule follows from the occurrence of a dimethoxyphthalic acid, amongst the products of the permanganate oxidation. *Metaemipinic acid*,  $\text{C}_6\text{H}_3(\text{OMe})_2(\text{COOH})_2$ , is a dibasic acid, and as it forms an *anhydride*, the carboxyl groups are adjacent, and it is a derivative of phthalic acid. Its molecule contains two methoxyl groups (§ 400), and as it is converted into protocatechuic acid (§ 310) when fused with potash, these methoxyl groups are adjacent. It is therefore either 1:2:3:4 or 1:2:4:5-dimethoxyphthalic acid; as, however, it forms only one *monomethyl ester*, it must be the symmetrical or 1:2:4:5-acid (compare Camphoric Acid, § 342).



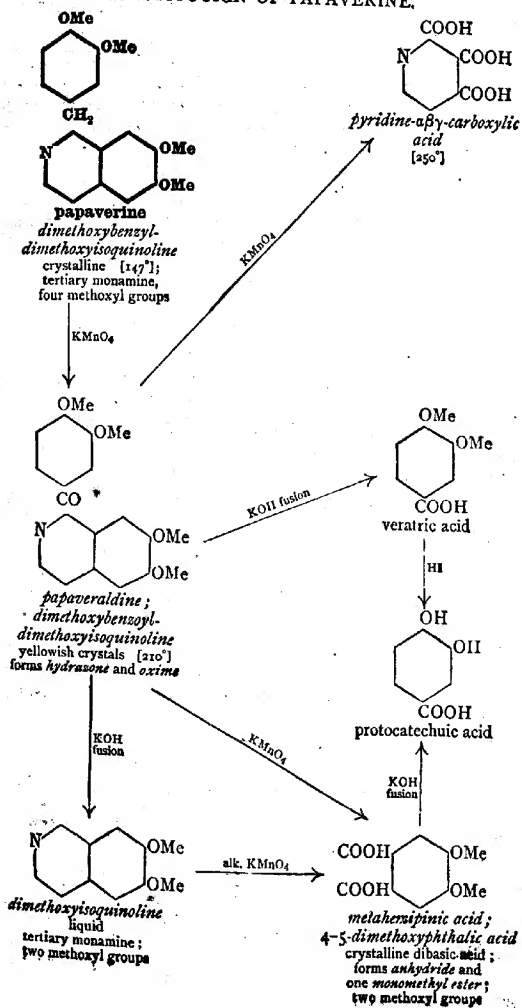
When narcotine is reduced with zinc and hydrochloric acid, it is resolved into a lactonic compound, *meconin*, and a simple base, *hydrocotarnine*, so that it is *meconin-hydrocotarnine*. Meconin is *dimethoxyphthalide* (§ 324), whilst hydrocotarnine is the methoxy-methyleneoxy-derivative of *N-methyl-tetrahydroisoquinoline*.

The reduced pyridine ring of narcotine and hydrocotarnine is broken by mild oxidation, with the result of forming *cotarnine*, which has been proved to be the corresponding alkyloxy-derivative of *o-methylamino-o-ethylbenzaldehyde*. It is interesting to note that the broken ring can be reconstituted by gentle reduction (compare Aminocinnamaldehyde, § 389), the cotarnine being reconverted into hydrocotarnine.



**405. Synopsis.**—Strychnine and brucine are quinoline derivatives; morphine and codeine are derivatives of tetrahydrophenanthrene, and papaverine and narcotine of benzylisoquinoline.

## CONSTITUTION OF PAPAVERINE.



## CHAPTER LXXIII

### THE THIOPHENE-PYRROLE AND OTHER HETERONUCLEAR GROUPS

**406. Thiophene: Furfurane.**—Commercial benzene from coal-tar invariably gives a blue coloration, when shaken with concentrated sulphuric acid containing a little isatin (or phenanthraquinone), but pure benzene from benzoic acid does not do so; and commercial benzene ceases to do so after it has been shaken repeatedly with small quantities of the acid.

The formation of this blue colouring matter, *indophenin*, is due to the presence of a cycloid sulphur compound, thiophene, which is very readily sulphonated.

As thiophene is formed by passing coal-gas over red-hot pyrites, it is probably synthesised in this manner from the pyrites, in the coal from which the aromatic hydrocarbons are prepared (compare § 243); it may be isolated from its *sulphonic acid* (compare § 247), obtained in the above manner from commercial benzene; and it may also be made synthetically by distilling a mixture of sodium succinate and phosphorus trisulphide, or of mucic acid (§ 183) and barium sulphide.

An analogous *selenophene* has been made having very similar properties.

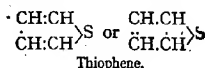
*Thiophene*,  $C_4H_4S$  (V. Meyer, 1883), is a colourless liquid, which boils at  $84^\circ$ , and resembles benzene in a most remarkable manner. Not only is it physically like benzene, but it forms a parallel series of derivatives which are scarcely distinguishable from the corresponding benzene derivatives.

*a-Bromothiophene* boils at  $150^\circ$ , bromobenzene at  $155^\circ$ . When boiled with methyl iodide and sodium, it is converted into *methylthiophene* or *thiotoluene*, a liquid resembling toluene, but boiling at  $113^\circ$ , instead of at  $111^\circ$ . This is oxidised by chromic acid mixture to *a-thiophene-carboxylic acid*, a substance which resembles benzoic acid, and boils at  $260^\circ$ , as against  $250^\circ$  (but  $K=0.0254$ ); the same acid is obtained by oxidising *acetothienone*, a crystalline substance which resembles acetophenone, and is formed similarly from acetyl chloride and thiophene in presence of aluminium chloride.

The various substituting agents, however, act much more readily on thiophene than on benzene, and the *sulphonic acid* is formed, even in the

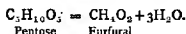
cold, with such energy that the thiophene must be diluted with benzene. Similarly in making *nitrothiophene*, the thiophene is best led into the acid in the form of vapour. The *dinitro-compound* is coloured red by caustic alkali, and its presence may thus often be detected in *m*-dinitrobenzene. *Aminothiophene* differs from aniline in that it does not form diazonium compounds, but it couples with diazonium salts, forming an azo-dye.

On account of its similarity to benzene, thiophene must be regarded as a ring compound, the molecule of which consists of a five-carbon benzenoid ring, in which a methylene group is replaced by a bivalent sulphur atom; this view is also borne out by its synthesis from succinic acid.



The oxygen analogue of thiophene is known as *furfurane*, its aldehyde being obtained when bran (*furfur*) is distilled with dilute sulphuric acid.

This aldehyde is formed quantitatively when xylose, arabinose, and other pentoses (§ 188) are distilled with hydrochloric acid; it is present in crude pyroligneous acid (§ 29), and in new bread; and its *bromomethyl-derivative* is formed by digesting fructose or cellulose with hydrogen bromide in ether.



*Furfural*,  $\text{C}_4\text{H}_3\text{O}.\text{CHO}$  (Fownes, 1845) is a colourless liquid of pleasant odour, boiling at  $162^\circ$ . It closely resembles the aromatic aldehydes; forms a crystalline *oxime*, *phenylhydrazone* and *bisulphite compound*; reduces silver, and is reduced by sodium amalgam; and is converted by caustic alkalies into the corresponding alcohol and acid.

The resemblance to benzaldehyde extends even to forming a green "*malachite*" dye with dimethylaniline, and a "*cinnamic*" acid with sodium acetate and acetic anhydride; but it is distinguished from benzaldehyde by yielding an intensely red compound with aniline salts.

*Furfuryl alcohol*,  $\text{C}_4\text{H}_3\text{O}.\text{CH}_2\text{OH}$ , which corresponds with benzyl alcohol, and is prepared by the action of caustic soda on the aldehyde, is a syrup which is coloured green by hydrochloric acid; it is also formed by the action of caustic soda on arabitol (§ 188).

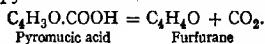
The acid which corresponds with furfural, and is formed by oxidising it with silver oxide, or, together with its alcohol, by the action of caustic alkali on the aldehyde, was originally obtained by distilling mucic acid (§ 183).

*Pyromucic acid*,  $\text{C}_4\text{H}_3\text{O}.\text{COOH}$  (Scheele, 1780), is a crystalline substance which melts at  $132^\circ$ , and sublimates at about the same

temperature;  $K=0.0707$ . It is distinctly less benzenoid than the aldehyde.

Although it forms *metallic salts*, and is convertible into a *chloride*, *amide* and *nitrile* in the same way as an aromatic acid, pyromucic acid combines additively with bromine vapour, forming a *tetrabromide*,  $C_4H_3Br_4O.COOH$ , which is oxidised to dibromosuccinic acid by chromic acid; it also decolorises cold alkaline permanganate, and behaves generally as an unsaturated compound.

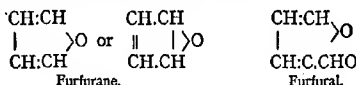
The mother substance of this group, furfuran, occurs with its aldehyde in the more volatile portions of wood tar, and is obtained when pyromucic acid is distilled with lime.



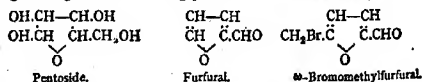
*Furfuran*,  $C_4H_4O$  (Limpricht, 1873), which is a colourless volatile liquid of characteristic odour, boils at  $32^\circ$ , and is only sparingly soluble in water; it is a very stable substance.

Hydrogen is not displaced from it by sodium, so that it is neither an acid nor an alcohol, and it does not form an oxime or hydrazone, so that it is not a ketone or aldehyde. The oxygen is therefore ethered; as is confirmed by its synthesis (by an ethereal condensation), when succinaldehyde (§§ 150, 407) is heated with water.

From the stability of its nucleus it must be concluded that furfuran is a ring compound analogous to thiophene, in the molecule of which the sulphur is replaced by an oxygen atom; in furfural and its derivatives the active group is therefore attached to the adjacent carbon atom.



The close relation between furfural and the pentoses is connected with the glucosidic structure (§ 181) of the latter; these sugars may in fact be regarded as derivatives of tetrahydrofurfuran, their conversion into furfural being analogous to that of glycerol into acrolein (§ 132).



Various furfuran derivatives can be made by direct synthesis. *aa'-Dimethylfurfuran*,  $(CH_3CMe)_2O$ , an insoluble liquid which boils at  $93^\circ$ , and resembles furfuran in properties, is made by distilling acetylacetone \* with zinc chloride,

\* *Acetylacetone*,  $CH_3.CO.CH_2.CH_2.CO.CH_3$ , which is a soluble liquid boiling at  $140^\circ$ , is made by boiling *ethyl diacetosuccinate*,  $COOEt.CHAc$ .

and is reconverted into this  $\gamma$ -diketone by hydrolysis with dilute hydrochloric acid at  $270^{\circ}$ .

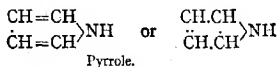
The furfuran compounds give a colour reaction resembling that of thiophene, a violet colour being formed when a member of this group is added to concentrated sulphuric acid, containing a little isatin or phenanthraquinone. Further, when a pine shaving moistened with concentrated hydrochloric acid is held in the vapour of a furfuran derivative, a green colour is developed.

**407. Pyrrole and Pyrrolidine: Indole.**—The nitrogen analogue of thiophene and furfuran is present in bone-tar oil and may also be made synthetically—as by heating ammonium mucate.

The pyridine bases having been removed by shaking with acid, and the fatty nitriles hydrolysed by boiling with alkali, the pyrrole is separated from the  $125^{\circ}$  fraction by boiling with solid caustic potash, which converts it into a solid *potassium derivative*; the base is liberated from this by boiling with excess of water.

**Pyrrole.**  $C_4H_4:NH$  (Runge, 1834), is a light colourless liquid, which boils at  $131^{\circ}$ , and resembles chloroform in odour; it soon turns brown in air, and is resinified by concentrated acids. Like thiophene and furfuran, it forms a dark blue product with isatin or anthraquinone and sulphuric acid, but it is especially distinguished by the fiery red colour (*πυρρος*) which its vapour imparts to a pine shaving moistened with hydrochloric acid; all pyrrole derivatives give some such colour.

Pyrrole is formed in quantity when succinimide is heated with zinc dust, and its constitution follows from this and similar relations.



Pyrrole is but a feeble base, and dissolves only slowly in dilute acids, and although one of its hydrogen atoms is displaceable by metallic potassium or potash, it is not affected by sodium; on warming its solution in dilute acid, an amorphous red colouring matter is precipitated, and ammonia is eliminated.

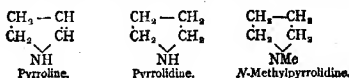
Like thiophene and furfuran, it forms various substitution products, the halogen derivatives being obtained with especial ease, as by the action of iodine and alkali. *Tetriodopyrrole*,  $C_4I_4NH$ , a deep yellow crystalline substance melting at  $140^{\circ}$ , is used as an antiseptic ("iodole"), instead of iodoform; it is equally efficient, but devoid of odour.

When pyrrole is reduced with zinc dust and acetic acid, it is converted into *pyrroline*,  $C_4H_7N$ , a soluble, alkaline liquid boiling at  $90^{\circ}$ ,

$CH_3Ac.COEt$ , with dilute soda; and this in turn is obtained by the action of iodine on ethyl sodacetoacetate (§ 144).

which condenses with hydroxylamine, forming succinaldoxime (§ 150).

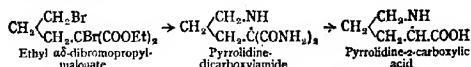
Pyrroline in turn may be still further reduced by hydriodic acid and phosphorus at a high temperature, to *pyrrolidine* or *tetramethylene-imine*,  $C_4H_9NH$ , which is a highly basic liquid, boiling at  $88^\circ$ . Pyrrolidine resembles piperidine in odour, and is formed synthetically in a similar manner by distilling tetramethylenediamine hydrochloride (§ 215); its *N*-methyl-derivative (§ 397), obtained by direct methylation, is similar.



Pyrrolidine-carboxylic acid is an important product of the hydrolysis of casein, albumen, gliadin, and other proteins (§§ 222, 224); the product thus obtained is *lævoglyrate*, but is accompanied by the racemised modification.

*l*-Pyrrolidine-2-carboxylic acid or *proline*,  $NH \cdot C_4H_7 \cdot COOH$  (Fischer, 1901), is a sweetish, slightly acid, crystalline substance, which melts at  $205^\circ$ ;  $[a]_D = -77^\circ$ . As the acid radical of this substance occurs frequently in natural and synthetic polypeptides (§ 223), it is conveniently termed the *prolyl* (i.e. pyrrolidine-carbonyl) radical (Fischer).

The *racemic acid* is also made synthetically by the action of ammonia on *ethyl α-dibromopropylmalonate*, which is obtained by brominating the corresponding *monobromo-ester*, formed by the action of trimethylene bromide (§ 288) with *ethyl sodiomalonate*; the *pyrrolidine-dicarboxylamide* thus produced is converted into the monocarboxylic acid by acid hydrolysis (carboxyl being eliminated).



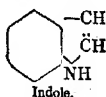
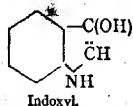
In connection with these pyrrolic protein derivatives, it is a significant fact that the pyrrole nucleus occurs in some of the vegetable alkaloids (§§ 397, 398), and bearing in mind the intimate connection between five-membered and six-membered cyclic compounds (§ 288), it seems not improbable that the pyrrole and pyridine alkaloids are formed naturally by the degradation of vegetable proteins (Pictet, 1903).

Like the benzene and pyridine rings, the thiophene, furfuran and pyrrole rings may form part of condensed-ring nuclei, analogous to those of naphthalene and quinoline.

*Coumarone*,  $C_9H_8 \cdot C_2H_2O$ , the benzene-furfuran compound (cf. Indole), is a liquid (b.p.  $169^\circ$ ), whilst *thionaphthene*,  $C_8H_6 \cdot C_2H_2S$ , the benzene-thiophene derivative, is a crystalline solid, resembling naphthalene.

The most important of these compounds is the benzene-pyrrole derivative, indole, which is the mother-substance of the indigo group (§ 338), and an essential constituent

of proteins (§ 222). It is obtained by distilling indigo or isatin with zinc-dust; indoxyl (§ 338) is  $\beta$ -hydroxyindole.

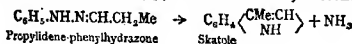


Indole,  $C_6H_4 \begin{smallmatrix} CH \\ NH \end{smallmatrix}$  (Baeyer, 1869) is a crystalline sub-

stance, which melts at  $52^\circ$ , and resembles  $\alpha$ -naphthylamine in odour; like pyrrole, it imparts a red colour to a pine shaving moistened with alcoholic hydrochloric acid. Indole is feebly basic, and is resinified by acids, but it forms a nitroso-compound.

$\beta$ -Methylindole or skatole, which is a similar crystalline substance melting at  $95^\circ$ , has a pronounced faecal odour, and occurs in faeces, from the bacterial decomposition of proteins.

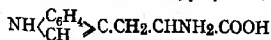
Skatole is also formed by fusing proteins with potash, and is easily prepared synthetically by heating propaldehyde-phenylhydrazone (§ 86) with zinc chloride. Indole- $\alpha$ -carboxylic acid is obtained similarly from pyrroacemic phenylhydrazone (§ 137), and the  $\alpha\beta$ -dicarboxylic acid from the  $p$ -xylylhydrazone.  $\alpha\beta$ -Dimethylindole, obtained by heating the latter, is also formed by condensing pyrrole with acetylacetone (§ 406).



The various indole derivatives obtained by the putrefaction or hydrolytic decomposition of proteins proceed from the degradation of indole-aminopropionic acid, to which the various protein colour-reactions (§ 222) are also to be attributed.

This compound is most readily obtained by fermenting casein with *trypsin*, the enzyme of the pancreas, and is separated from the accompanying cystine and tyrosine (§§ 220, 335) by fractional precipitation with mercuric sulphate in acid solution. It has also been isolated from egg-albumen, and from *gliadin*, the protein of wheat.

Indole-aminopropionic acid or tryptophane,



(Hopkins, 1901), which is a soluble, acid, crystalline substance, melting at  $252^\circ$ ,  $[a]_D = -33^\circ$ , forms an intense purple with glyoxylic acid, in presence of sulphuric acid (§ 121), and a characteristic rose-red with bromine water; it is converted into skatole by fusion with potash, and into indole-acetic acid by bacterial hydrolysis.



The benzene-pyrrole compound analogous to anthracene, occurs with that hydrocarbon in coal-tar, from which it may be isolated by means of its *potassium derivative*, in the same way as pyrrole from bone-oil.

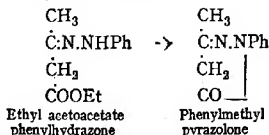
*Carbazole*,  $C_8H_7NH \cdot C_6H_5$ , is a feebly basic, crystalline substance, which melts at  $238^\circ$ , and boils stably at  $352^\circ$ ; it may be made synthetically by heating diphenylamine to redness.

**408. The Azoles.**—Many compounds have been synthesised in which the methine groups of the pyrrole and allied rings are replaced by nitrogen; they are termed *azoles*.

Such rings are usually formed by condensing amino-compounds with aldehydes or ketones: but although the number of such considerations is very large, few as yet are of other than theoretical interest.

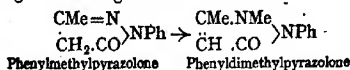
*Pyrazole*,  $\begin{matrix} CH-N \\ CH-CH \end{matrix} > NH$ , which is the dinitrogen analogue of pyrrole, is a crystalline substance, formed by condensing epichlorhydrin with hydrazine hydrate; it is feebly basic, and forms a *silver compound* analogous to potassium-pyrrole. The well-known drug, antipyrine, is the phenyldimethyl derivative of a related ketone, *pyrazolone*.

Phenyl-dimethyl-pyrazolone ("antipyrine") is made synthetically, by the successive action of phenylhydrazine and methyl iodide on ethyl acetoacetate,



The ketonic ester condenses with the hydrazine, probably forming a hydrazone in the normal manner; but the imino-group of the latter at once interacts with the ester group at the other end of the chain, and an amino-compound is formed with elimination of alcohol, as in the formation of acetamide from ethyl acetate. The product is of course a ring compound, as the interacting groups are attached to the same chain.

On heating the crystalline *phenylmethylpyrazolone* with methyl iodide and methyl alcohol, at  $100^\circ$ , it is at once converted into antipyrine, the molecule at the same time undergoing a slight rearrangement.



*Phenyldimethylpyrazolone*,  $\begin{matrix} CMe.NMe^2 \\ CH.CO \end{matrix} > NPh$  (Knorr, 1883), is a colourless, crystalline substance melting at  $114^\circ$ ; it is freely

soluble in water and alcohol, and is used as an antipyretic. This synthetic alkaloid is a powerful monacid base, and generally resembles the pyridine alkaloids.

*Lysidine* or *methylpyrazoline*,  $\begin{matrix} \text{CH}_2\text{N} \\ \text{CH}_2\text{NH} \end{matrix} > \text{CMe}$ , a crystalline substance melting at  $105^\circ$ , is formed by heating ethylene-diamine hydrochloride (§ 215) with sodium acetate; it is used in medicine by reason of the solubility of its *urate*.

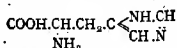
*Triazole*,  $\begin{matrix} \text{CH:N} \\ \text{N:CH} \end{matrix} > \text{NH}$ , which is an almost neutral substance melting at  $121^\circ$ , is made by condensing formamide with *formyl-hydrazine*

*Tetrazole*,  $\begin{matrix} \text{CH:N} \\ \text{N:N} \end{matrix} > \text{NH}$ , which melts at  $156^\circ$ , is made by eliminating the amino-group from its *amino-derivative*, which is formed by the protracted action of nitrous acid on guanidine-diazonium nitrate (§§ 247, 258).

*Glyoxaline* or *iminoazole*,  $\begin{matrix} \text{CH:CH} \\ \text{N:CH} \end{matrix} > \text{NH}$  (Debus, 1856), a crystalline substance melting at  $90^\circ$ , is formed by the action of ammonia on glyoxal, preferably in presence of formaldehyde; it is a moderately strong secondary amine, and forms stable salts. *N-Methylglyoxaline*, formed by direct interaction with methyl iodide, is a crystallisable liquid boiling at  $199^\circ$ .

Histidine, the principal representative of the "hexone" bases, is an important degradation product of proteins; it is formed by the acid hydrolysis of most members of this class (§ 222), and is most readily obtained in this manner, from protamines such as sturine (§ 223).

*Histidine*,  $\text{C}_8\text{H}_9\text{N}_3\text{O}_2$  (Kossel, 1896), is a crystalline substance which is freely soluble in water, but only sparingly so in alcohol; its reactions show that it is an amino-acid, and as it is stable towards concentrated nitric acid it is probably a glyoxaline derivative, *glyoxaline-aminopropionic acid*.

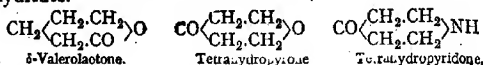


Probable Structural Formula of Histidine.

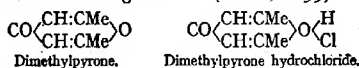
#### 409. Pyrone and Pyridone Derivatives: Oxonium Compounds.—

The ring compounds of the type of furfuran, pyrrole and pyrazole, are built on nuclei containing five linked atoms, in distinction from compounds of the pyridine group, which are based on six-membered rings. The pyridone compounds are  $\gamma$ -ketonic derivatives of piperidine, and the pyrone compounds bear the same relation to them as furfuran to pyrrole. These six-membered oxygenated ring-compounds are also intimately

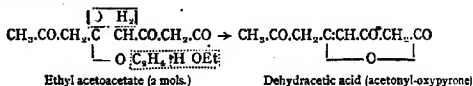
connected with the aliphatic  $\delta$ -lactones (§ 151), and carboxylic anhydrides.



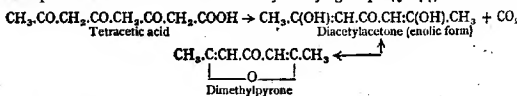
The principal compound of this group, dimethylpyrone, is made synthetically from ethyl acetoacetate; it is of especial interest as a basic, oxonium compound, in the molecule of which a bivalent oxygen atom, becoming quadrivalent, combines additively with acid radicals, in the same way as an aminoid nitrogen atom\* (Collie, 1899).



When ethyl acetoacetate is persistently heated, it is converted into a condensation product, dehydracetic acid (§ 143), alcohol and ethylene being eliminated.



Dehydracetic acid or tetracetic lactone is a crystalline substance melting at  $109^\circ$ ; when boiled with concentrated hydrochloric acid, it is rapidly converted into dimethylpyrone hydrochloride. The lactonic carboxyl group is eliminated, yielding diacetylacetone (below); and a new condensation takes place between the two enolic hydroxyl groups (§ 144) of the latter.



Dimethylpyrone hydrochloride,  $\text{C}_7\text{H}_8\text{O}_2\text{HCl} \cdot 2\text{H}_2\text{O}$ , is a crystalline substance melting at  $85^\circ$ ; its solution is strongly acid, and yields dimethylpyrone itself when shaken with chloroform, but the salt itself is stable, and may be prepared directly from the base. The *platinichloride*,  $(\text{C}_7\text{H}_8\text{O}_2\text{HCl})_2\text{PtCl}_4$ , is also of aminoid type, and several other stable, well-defined salts have been prepared, such as the *oxalate* and *nitrate*.

Dimethylpyrone,  $\text{C}_7\text{H}_8\text{O}_2$ , which is a crystalline substance melting at  $132^\circ$ , sublimes easily and is very soluble in water. When heated with baryta water it is hydrolysed to *diacetylacetone*,  $\text{CO}(\text{CH}_2\text{COCH}_3)_2$ , a crystalline substance melting at  $49^\circ$ , from which it is again obtained by heating.

Although dimethylpyrone is interconvertible with diacetyl-

acetone, it has none of the properties of an open-chain ketone; and the fact that it forms stable salts is best explained on the above oxonium hypothesis, which also accounts for the existence of such compounds as *dimethyl ether hydrochloride*,  $(\text{CH}_3)_2\text{O}, \text{HCl}$ .

Diacetylacetone and dehydracetic acid are converted by ammonia into *dimethylpyridone* or *lutidone*, a crystalline substance melting at  $225^\circ$ ; this is a stronger base than dimethylpyrone, but its salts are of precisely the same type; the synthetic drug *eucaine* (§ 393), is an important derivative.

Many pyrone derivatives have been prepared; *meconic acid*, for example, (§ 403) is an *oxypyrono-dicarboxylic acid*.

410. *Synopsis*.—Many ring compounds are known, in which nitrogen, sulphur, or oxygen take the place of some of the carbon atoms.



## APPENDIX

### SUPPLEMENTARY LABORATORY NOTES

*This appendix consists of notes which, taken in conjunction with the text form a complete laboratory course. It should be clearly understood that these notes are supplementary to the text, and are only complete when taken in conjunction with it.*

#### PLAN OF WORK

Before commencing work, each chapter should be carefully studied, and the necessary apparatus and materials collected. Progress will be slow at first, but speed will come with experience. Progress is much accelerated by writing out a careful account of each piece of work as soon as it is finished, comparing the results and yields actually obtained with the standard results; the yields indicated are the percentage proportion of the theoretical yield usually obtained (compare § 64, Text; and § 20, Appendix). If an experiment fails, it saves time in the long run to repeat it; a careful worker learns even from a failure.

It is recommended to work through the book in the order given, to the end of Part I. Parts II. and III. should then be taken concurrently. The experiments enclosed in square brackets are more complicated, and should be left until after the others. It is advisable to read ahead, and especially to note what materials are required, or the work may be delayed while the materials are being made or procured. When a preparation has to be kept, some days before proceeding further, the early stages should be taken in advance, before the preceding experiments are completed.

#### LIST OF APPARATUS

Retort stand with three rings and adjustable clamp for condenser. Tripod and wire gauze. Sand bath. Tin plate saucepan, 5 inches diameter, for water bath. 6-oz. distilling flask. Ordinary flasks, 2-oz., 4-oz., 6-oz. Large wash bottle, fitted. Corks to fit flasks, test tubes, condenser, etc. Set of three cork-borers. Rat-tail file. Thermometer with paper scale to 250°. Bunsen burners and tubing. 100 cc. graduated measuring cylinder. 30-inch Liebig's condenser, and  $\frac{1}{4}$  inch indiarubber tubing. Quadrant brass photographic balance with glass pan, weighing from 1 to 50 grams.\* Two porcelain crucibles and lids. Pipeclay triangle. Crucible

\* These little folding balances are inexpensive, and weigh accurately to  $\frac{1}{2}$  gram; care must be taken to level the index to zero before use.

tongs. Blowpipe. Platinum foil and wire. Test-tube stand. Twelve large and twelve small test tubes. Test-tube brush. Three beakers, 4-oz., 6-oz., 8-oz. Three funnels, 2-inch, 3-inch, 4-inch. Two packets of filters, 4-inch, 6-inch. Two thistle funnels. Three watch-glasses. Two porous tiles or 6-inch white plates (cheese plates), unglazed. Glass tubing: soft,  $\frac{1}{2}$  inch diameter; hard,  $\frac{1}{4}$  inch diameter. Glass rods. Three-cornered file. Glass filter pump. Stout 500 cc. bottle with neck  $1\frac{1}{2}$  inch diameter, and paraffined cork to fit, to take funnel for pressure filtering (or Buchner funnel and flask). Pestle and mortar. Stoneware pneumatic trough and beehive shelf.

Students are recommended to work in couples. If working alone, some of the above apparatus will be required in duplicate.

## PART I

### CHAPTER I

(The numbers of the paragraphs correspond with the section headings.)

3. *Distilling Apparatus.*—Fit the thermometer to a 6-oz. distilling flask through an ordinary well-rolled cork (*not* paraffined, and bored accurately and smoothly), the *top* of the bulb being just *below* the side tube. (Rubber stoppers are undesirable as they are attacked by so many organic liquids; corks may be rendered acid proof by painting them with chromo-gelatine—2 grams gelatine in 20 cc. hot water, to which is added 0.5 gram bichromate in 5 cc. hot water—and then exposing them to daylight for some days.) The flask rests on wire gauze, supported by a tripod or ring, and no further support is necessary if the cork to the condenser tube fits well and is bored accurately; the side-tube of the flask should be pushed as far as possible into the condenser (see Frontispiece). The other end of the condenser projects *loosely* into an ordinary flask, which should rest on the bench and not on blocks, etc. The cooling water is passed into the *lower* tubulure of the condenser jacket, and on escaping from the upper tubulure should be just warm; only a *small stream* is required for ordinary distillations. The rubber joints between the condenser tube and jacket must be quite water-tight.

3. *Distillation of Wine or Beer.*—Distil 50 cc. of wine or 100 cc. of beer; the flask not more than two-thirds full. Heat with *small flame*, and *steadily*, otherwise bumping may occur; if the liquid bumps persistently, put in two or three *small pieces* of unglazed porcelain (broken pipe clay or porous plate), first cooling. If it froths over, as it probably will do with beer, redistil the distillate until a clean liquid is obtained. Prove the first part of the distillate has a low boiling point, and is inflammable.

4. *Boiling Point.*—As the thermometer stem is not entirely in the vapour, the reading is too low; for very accurate work add  $N(T-t) \times 0.00015$ , where  $N$ =no. of degrees unimmersed,  $T$ =reading of thermometer, and  $t$ =temperature of second thermometer half way between top of mercury and cork; it is better to use a long-necked flask or short thermometer. As the boiling point is the temperature of the vapour when given off freely under the standard atmospheric pressure, the height of the barometer must be noted; the rough correction for common organic liquids is  $1^\circ$  for each 35 mm. difference from 760 mm. Take care that the thermometer is not superheated, e.g. by too large a flame; it should drip slowly with condensed liquid, so that the cotton-wool covering is always wet; this covering should be as thin as possible, and will adhere to the bulb if twisted tightly. Check the accuracy of the thermometer



once for all by distilling 100 cc. of water (or other pure liquid of known boiling-point) through the apparatus, and note the correction for future use. The boiling-point of a liquid is always determined in this way, *never* by placing the thermometer bulb in the liquid; if the liquid is a mixture, distil steadily until a constant boiling-point is attained.

4. *Specific Gravity*.—The ordinary bottle method is good enough for most purposes: a 5 cc. bulb is blown on a glass tube, which is drawn out in the middle of the neck, and marked lightly with a file at the narrow part. Weigh empty— $w_1$  (a balance weighing to 1 milligram is required). Fill with distilled water (with a fine pipette), immerse in water of known temperature (properly 4°, but that of water supply will do), and adjust to the mark with pipette or filter paper. Dry outside and weigh— $w_2$ . Weight of water =  $w_2 - w_1$ . Repeat, and note these data once for all. Next thoroughly rinse with liquid, or best of all, dry the flask by sucking air through it with the pump and warming. Fill with liquid, and adjust as before, *at the same temperature*. Replace stopper and weigh— $w_3$ . Then weight of liquid =  $w_3 - w_1$ , and sp. gr. at  $t^\circ = (w_3 - w_1) / (w_2 - w_1)$ .

4. *Fractional Distillation*.—First fractionation: Use a *small flame*, and keep boiling *steadily*: watch the thermometer, and change the receiver as the mercury passes each temperature limit, *but do not alter or take away the flame*. Measure the fractions. Second fractionation: Clean out the flask, replace the *first* fraction, and resume the distillation, using a *small flame* as before. When the first limit, 82°, is again reached, some liquid now remains in the flask; *stop boiling* for a moment, and add the second fraction to this. Now resume the distillation, *but do not change the receiver*; some liquid now comes over below 82°, which collect *in the same receiver*. When the limit is again reached, stop for a moment and add the third fraction, again *without changing the receiver*. On resuming, still a little distils below 82°, and possibly also on adding the fourth and fifth fractions in the same way. When the distillate from the *fifth* fraction reaches 82°, *do not stop boiling, but change the receiver, and then proceed exactly as in the first fractionation*. Measure the fractions. Third fractionation: Exactly the same as the second; measure the fractions, and take the sp.gr. of the head and tail fractions. Note that the head fraction is inflammable; keep it for testing (§§ 18, 19). Note that the tail fraction can be frozen (place a few drops in a small test-tube, standing in a small crucible containing strong ammonia, through which blow air with a long pipette).

5. *Absolute Alcohol*.—Boil 300 cc. methylated spirit in a reflux apparatus (Fig. 2) with 10 grams caustic soda for 1 hour (if pure spirit is available, this stage may be omitted); the narrow end of the condenser should project *at least an inch beyond the cork*, which it should fit accurately. The flask is heated on a water bath, i.e. saucepan of boiling water, rather less in diameter, so that it is heated by the steam. Then fit the flask with a wide bent tube leading to a condenser (Fig. 2), and distil *on the water bath, as long as anything passes over*; there is no danger of cracking the flask if water is kept in the saucepan. Use as receiver a similar flask, containing 140 grams of *fresh* quicklime (see first that a lump of this heats with water, and falls to pieces); the spirit and lime should not more than half fill the flask, or the lime in swelling up will burst it. Connect the receiving flask, containing the lime and purified alcohol, with the inverted condenser, and either leave for 24 hours or boil in the water-bath for an hour; in the latter case watch the operation at first, as the action is apt to be violent. Finally arrange for distillation, using the wide bent tube, and distil again

from the water-bath, without pouring off the liquid from the lime, or transferring it to a second flask; distil as from the soda until no more passes over. Redistil 50 cc. of the product in the ordinary apparatus, and note the b.p.; this should soon be quite steady with rectified spirit, but will continue to rise slowly (76–78°) with methylated spirit. Yield 80 per cent. Take the sp.-gr. of early and late samples; this should be constant (with the same reservation). The product thus obtained contains 2 to 3 per cent. of water; this may be reduced to less than 1 per cent. by repeating the treatment with quicklime, using only 70 grams.

6. *Chemical Tests of Purity.*—Anhydrous copper sulphate is made by heating a blue crystal gently in a porcelain crucible, until it crumbles; it should not be heated so strongly as to show the brown oxide. Other tests as directed.

## CHAPTER II

9. *Detection of Carbon and Hydrogen.*—Burn some absolute alcohol on a watch glass beneath a funnel, which is connected through two flasks or test tubes with an inverted wash bottle of water, or a water pump (Fig. 9, § 25). Prove the presence of moisture in the first (keep cool) by copper sulphate, and carbon dioxide in the second by lime water.

[9.\* *Carbon and Hydrogen Combustion.*—Hard glass tube 90 cm. long, 1.5 cm. internal diameter, cut off cleanly at ends; widen slightly, and smooth in the blowpipe; thoroughly clean and dry, and embed in asbestos in the furnace trough, the ends protruding about 5 cm. beyond the end of the trough. Singly-bored rubber corks at both ends, well dried and blackheaded to prevent sticking when hot. The drying apparatus (Coram's, Fig. 3) is convenient if much work is to be done, but ordinary wash-bottles and U-tubes will serve; concentrated potash, 1 in 5 (not soda, as the carbonate is less soluble), followed by concentrated sulphuric acid, both distributed over small pumice. In the combustion tube, starting from the air end: (a) 25 cm. empty for boat; (b) 45 cm. with copper oxide, granulated, or from wire (dried over a flame, as it is hygroscopic), kept in position by 1 cm. loose rolls of copper gauze; (c) 20 cm. empty. Water-collecting tube as shown, with sulphuric acid and pumice; whatever drying agent is used must be used throughout the apparatus. The potash bulbs (Geissler's pattern) are half filled with 1 in 5 solution, the upper tube with pumice moistened with sulphuric acid. A U-tube of soda-lime (freshly dried in an iron dish over a small flame) may be substituted for the potash; the attached drying tube is then a small U-tube constricted at the bottom, to show the rate at which the gas is passing. The absorption apparatus is protected from the heat of the furnace by a large asbestos screen, as shown.

Begin with a blank experiment in a dry air stream, without the boat. Heat the copper oxide gradually, and when moisture has for some time ceased to appear at the end of the tube, place the weighed absorption tubes in position, and continue until the tubes cease to increase in weight. They must remain in the balance case for half an hour before each weighing, capped with short pieces of rubber tube and rounded fragments of glass rod (removed during the actual weighing).

\* Experiments in square brackets should be deferred.

When the apparatus is in working order, make trial combustions of sugar candy, or recrystallised oxalic acid, using quantities as indicated for alcohol. The copper oxide being red hot, the platinum (or porcelain) boat is weighed, empty and with solid (weigh again at the end, to prove that there is no residue), and pushed into the empty space reserved, followed by a cold, recently ignited, 5 cm. roll of copper gauze; this prevents the backward passage of gases; it should just fit the tube, but be well clear of the boat. Reconnect, and heat this roll to redness; then warm the boat with a single burner (small flame), passing air at one bubble per two seconds; as soon as the rate increases owing to the combustion, check the air supply; little gas escapes at this stage, the carbon dioxide being absorbed. As the combustion proceeds, the air supply is again slightly accelerated, but the rate through the absorption apparatus must not exceed that stated. Towards the end of the operation, the boat is heated to dull redness (if a charred residue should persist, pass oxygen until it disappears; but this is rarely necessary). Finally, pass air for 15 minutes after the complete disappearance of the solid.

In a series of combustions, the copper oxide need not be cooled,\* but only the boat end of tube; if two sets of absorption tubes are kept, the next combustion may be started forthwith. Practise as above until concordant results are obtained.

[For the analysis of alcohol, make a little bulb with a long thin neck, of such size that the bulb will rest in the boat, and the neck project a little over the end. Weigh the bulb empty and quite dry, then introduce about the right amount of liquid by warming, allowing the neck to dip into the liquid and then cooling. Then weigh; the end need not be fused if the liquid is carefully driven out of the neck before weighing. When the combustion apparatus is in order, place the bulb in the boat with the neck-end forwards, push it *quickly* into the combustion tube, and replace the copper roll and stopper. The heating must be *exceedingly cautious*, or the vapour will come off too fast; a hot tile over the boat serves very well; at the end of the operation the bulb must be quite empty.]

[12. *Vapour Density with Victor Meyer's Apparatus.*—The vapour of the jacketing liquid should not quite reach the cork. A few cc. of mercury must be placed in the displacement tube, or the tube of substance in falling will break it. The substance is weighed in a small stoppered tube, supplied with the apparatus. When the experiment is finished, and no more gas is displaced, remove the cork of the displacement vessel before stopping boiling, otherwise water will be forced back from the pneumatic trough. Vapour pressure of water = 9.1 mm. at 10°, 12.7 mm. at 15°, 17.4 mm. at 20°, 23.5 mm. at 25°; for intermediate temperatures take as proportional. Clean and dry the inner tube before each experiment.]

[14. *Molecular Weight by Cryoscopic Method.*—Approximate results can be obtained with a good physical thermometer graduated in tenths or fifths of a degree. In Beckmann's apparatus (which is that usually employed), the thermometer is differential, having a very large bulb and a very narrow bore, with an additional reservoir at the top. The scale is about 6° only, divided into  $\frac{1}{100}$ °, so that mercury must be passed into or withdrawn from the upper reservoir, until the column stands near the top of the scale at the required temperature.]

[14. *Molecular Weight by Boiling Point Method.*—The vapour pressure of a liquid is lowered by the presence of an indifferent dissolved substance, and its boiling point therefore raised. The relation is indicated by the

equation  $M = KP/E$  (compare cryoscopic formula), where  $M$  = mol. wt. of dissolved substance,  $P$  = no. of grains dissolved in 100 grams of solvent,  $E$  = elevation of b.p., and  $K$  = constant for solvent (5.2 for water, 25.3 for acetic acid, 26.7 for benzene);  $K$  is also equal to  $T^2/50L$ , where  $T$  is the absolute b.p. of the solvent, and  $L$  its latent heat of evaporation at its b.p. The thermometer bulb must be in the solution, and the vapour of the solvent must be returned by a reflux condenser or the concentration will be altered. Beckmann's special apparatus is the most convenient.

A better result is obtained by passing the vapour of the boiling solvent (generated in a separate small flask) into a solution of a weighed quantity of the substance in a weighed quantity of the solvent, contained in a large test-tube jacketed with the vapour of the solvent. A steady boiling-point having been obtained, the increase in the amount of the solvent is determined by weighing.]

### CHAPTER III

16, 17. *Sodium Ethoxide*.—Add 2 grams dry, bright sodium to 30 cc. dry alcohol; drain the crystals of alcoholate on a porous plate, as they are deliquescent. Heat the drying tube in melted paraffin wax, and dry the coal gas with sulphuric acid. Tests: flame; copper oxide (carbon dioxide by lime water; water by copper sulphate). Keep the dry ethoxide in a well-corked tube, as it is very hygroscopic.

18, 19. *Hydrolysis of Sodium Ethoxide*.—Distil 5 cc. from a solution of 3 grams ethoxide in 30 cc. water, using a flame under gauze. Add a stick of soda, cork (not too tightly) and leave. In a few hours a layer of alcohol can be pipetted off (a very fine pipette—capillary pipette—should be used, with rubber suction tube); burn some and test some by the iodoform, aldehyde and ethyl acetate tests. Test also some untreated spirit, and the head fraction from the beer (§ 3).

19. *Qualitative Tests for Alcohol*.—The iodoform test is very delicate; add a drop of spirit to some water, make almost black with iodine in potassium iodide, add caustic soda cautiously until colour has almost disappeared, warm gently. Yellow crystalline precipitate or turbidity of iodoform; the odour may be apparent, even if there is not enough to give a turbidity. The aldehyde test is fairly delicate: warm the liquid with two or three drops of potassium dichromate solution and a little dilute sulphuric acid; the chromate is reduced to green chrome alum, and the alcohol oxidised to aldehyde, which has a peculiar, pungent odour. The ethyl acetate test is not very delicate: mix the liquid with a few drops of acetic acid and twice its volume of concentrated sulphuric acid, and warm if necessary; the ethyl acetate has a fruity, pleasant odour. *Always make all three tests.*

20. *Ethyl Bromide*.—Flask, condenser and receiver should be quite dry. 6 grams red phosphorus and 50 cc. dry alcohol in flask, cooled with water. Add *very slowly* from a tap-funnel (its end not touching the alcohol), 14 cc. bromine; a few drops only at a time, each time *thoroughly shaking*, allowing to become warm, and then cooling. *If these precautions are neglected there will be an explosion.* Keep overnight if possible, well corked. Use only small quantities of water, etc., for washing, and

when the heavy bromide is *quite free from floating drops*, add 2 or 3 small pieces of fused calcium chloride. *Pour off from this before distilling*, and avoid loss by volatilisation. Yield 25 per cent.\* Note b.p., sp-gr. No precipitate with silver nitrate until warmed with alcohol.

[20. *Ethyl Bromide* (in quantity).—A much better yield is obtained by the potassium bromide method. Add 28 grams potassium bromide to a cold mixture of 15 cc. concentrated sulphuric acid and 25 cc. spirit, and distil cautiously from a sand-bath; purify as before. Yield 70 per cent.]

[20. *Ethyl Iodide*.—Place 20 grams of iodine in a distilling flask, connected with a condenser, add 12 cc. dry alcohol, and then, cooling with water, 2 grams dry, red phosphorus (allow the mixture to become warm, but not so much as to cause distillation). Mix well, and keep corked until next day. Distil from a water-bath, and purify as with the bromide. Redistil when dry, and note b.p. Yield 75 per cent. Precipitated slowly on shaking with aqueous silver nitrate, and immediately by an alcoholic solution. Ethyl iodide can be kept colourless by a few pieces of bright copper wire.]

21. *Qualitative Tests for Halogens*.—Green-edged flame when burned; green flame coloration with large fragment of granulated copper oxide mounted on platinum wire; the oxide is first heated to redness until the flame ceases to be coloured, and when cool is moistened with the liquid. An alternative method consists in carefully dropping some of the substance (using a fine pipette, if liquid) on a fragment of *pure* quicklime (made by heating a fragment of marble strongly, in the blowpipe on platinum foil) in a *small* hard-glass tube, and then heating to redness for a minute; the heavy vapour interacts with the lime, which is then cooled, dissolved in dilute nitric acid, and tested for halogen.

[21. *Estimation of Halogen*.—Stout thick-walled, soft-glass tube about 10 inches long, one end rounded, 1 gram powdered silver nitrate and 4 cc. concentrated nitric acid are introduced through separate funnels, without soiling the upper part of the tube; then the substance (whether solid or liquid) in a sealed thin-glass bulb (a solid may be placed in a narrower tube about 2½ inches long, sealed at one end; this will adhere to the wet sides of the tube, and remain about half way down). The tube is then carefully drawn out, *with well-thickened walls*, at a short distance from the open end, and is carefully sealed, *with thick and well-annealed walls*. The bulb containing the substance is next broken by shaking briskly, and the tube placed in the furnace. Heat is applied gradually, first 100°, and so on, for an hour or so at each stage. The ends of the furnace must face a brick or iron screen, to prevent damage should the tube explode; if much gas is expected it saves time, after heating at 100°, to cool, open and reseal. To unseal the tube, it is slipped *cold* out of the oven, and wound round with a cloth as it appears; any drops of liquid at the narrow sealed end are then removed by cautiously holding near a hot tile, and the end is softened in a flame; the sealed end is held away from the operator, and the tube is well wrapped up and held firmly. When the oxidation is complete the silver haloid lies at the bottom of the clear liquid; after unsealing, the tube is cut just below the narrow part, and rinsed into the beaker to which the precipitate and liquid are trans-

\* Unless explicitly stated otherwise the yields are expressed in percentages of those required by the assumption that the action proceeds quantitatively and in one direction only.

ferred. The silver bromide, etc., is collected on a filter, and washed and transferred to a porcelain crucible in the usual way; or the residual silver nitrate may be titrated by the thiocyanate method. *The student is warned not to attempt sealed tube work without supervision, as explosions happen in the most experienced hands.*]

22. *Hydrolysis of Ethyl Bromide or Iodide.*—Boil 5 cc. with 5 grams of caustic soda in 25 cc. of water. Ordinary flask without side-tube (Fig. 8); narrow end of condenser projecting into neck at least an inch beyond cork; isolate and test alcohol as in §§ 18, 19 (distil over a flame); prove the residue contains sodium halide. For bumping, see § 3.

23. *Ethyl Chloride.*—Fit a test-tube with a cork, and a short tube drawn out to form a gas-jet; place in it some common salt, cover with alcohol, and add an equal bulk of concentrated sulphuric acid; warm if necessary. The ethyl chloride vapour burns with a green flame.

[23. *Ethyl Chloride* (in quantity).—Add 40 grams zinc chloride to 100 cc. spirit, and saturate cold with acid (from charges of 100 grams salt, warmed with a mixture of 100 cc. sulphuric acid and 20 cc. water). Then boil in a paraffin bath, and pass in more gas as long as chloride is formed; condense in U-tube immersed in ice and salt. Yield 50 per cent. No turbidity with silver nitrate, even in alcoholic solution.]

#### CHAPTER IV

23. *Ethyl Sodium Sulphate.*—Pour 35 cc. sulphuric acid carefully into 100 cc. rectified or methylated spirit, shaking constantly. Heat in an open flask on a water-bath; then cool, dilute to 500 cc. and neutralise with whitening (an earthenware pneumatic trough is convenient for this purpose). Filter with suction, using a Buchner funnel and pressure flask, connected through thick-walled rubber tube (or glass tube with very short rubber joints) with the water pump (Fig. 9); a fair water-pressure is necessary. If a Buchner funnel is not available, use a large glass funnel, fitted to a strong, wide-necked bottle; the filter must fit well, and be supported by a second small, waxed filter, pierced with pin-holes.

Precipitate the lime with washing soda solution, *taking care to avoid excess*; the product *should not be alkaline*, nor effervesce with acids; it is therefore best to reserve some of the original solution in case of over-neutralisation. Drain the crystals on a porous plate. Yield 20 per cent.

*Recrystallise from Alcohol.*—Add hot alcohol cautiously to half the product (keeping hot on a water-bath) until it is just dissolved; then add half the remainder, followed by more alcohol in the same manner; finally (reserving only a few crystals) add the balance. Boil, filter quickly through a pleated filter in a truncated funnel (if the neck is not removed, it becomes choked with crystals); allow to cool, pour off the mother liquor, and drain the crystals on a porous plate. (To pleat a filter, fold as usual, open to semicircle, and fold each double quadrant *inwards*, so that its straight edge meets the vertical middle line; then double *each* of the four half-quadrants *outwards* upon itself, forming a narrow, wedge-shaped packet of quarter-quadrants—22½°; *press tightly*, open out, and place the fanlike cone loosely in the funnel.)

23. *Qualitative Test for Sulphur.*—Heat the solid with sodium on a

scrap of porcelain, or in a small test-tube; the black precipitate should not be dissolved by dilute hydrochloric acid.

[25. *Estimation of Sulphur*.—As halogen, but without silver nitrate; dilute well before precipitating. In this particular case the ethyl sulphates might be hydrolysed by boiling with dilute hydrochloric acid, and the sulphuric acid at once precipitated; or the sodium salt might be fused with sodium carbonate and nitre; but the first process is applicable to all organic sulphur compounds.]

[21, 25. *Estimation of Carbon and Hydrogen in Compounds containing Halogen or Sulphur*.—If halogen is present, a 10 cm. roll of silver gauze is placed after the copper oxide, and a similar 5 cm. roll before the boat, instead of the copper roll. The longer roll must be kept at a bright red heat; the silver halide sublimes on the combustion tube, leaving the roll clean and bright. The chromate method is less convenient.

If sulphur is present, the copper oxide is replaced by fused and coarsely crushed lead chromate, and the substance mixed with five or six times its weight of the finely powdered chromate in a large iron boat, or simply in the tube; the chromate must not be heated too strongly or it will fuse; it may be mixed with potassium dichromate to raise its melting-point. The sulphur is converted into non-volatile lead sulphate.]

25. *Hydrolysis of Ethyl Sodium Sulphate*.—Dissolve 5 grams sulphate in 50 cc. water with enough sulphuric acid to make the solution distinctly acid; distil at once. Apply iodoform, aldehyde and ethyl acetate tests, and evaporate residue for sodium hydrogen sulphate, which test.

26. *Ether*.—Ether is very volatile, and its vapour very heavy and inflammable; in working with it, keep all flames away from the receiver, etc., and in redistilling it, use hot water, heated away from the apparatus. Heat 20 cc. spirit with 20 cc. concentrated sulphuric acid in a distilling flask, and when the temperature reaches 140°, run in 80 cc. spirit at such a rate as to keep the temperature (which would otherwise rise rapidly) at 140–145°; the supply is controlled by means of a screw pinchcock on the rubber tube attached to the shorter tube, and the spirit must be delivered beneath the surface. Yield 75 per cent. B.p.; sp.gr.; heaviness of vapour (pour into beaker on balance); inflammability; carbon dioxide left in beaker on burning the vapour.

[26. *Drying Ether*.—Place 1 gram of bright slices of sodium in 10 cc. ether, well-dried with calcium chloride (in reflux apparatus); there is a brisk effervescence (owing to the decomposition of the residual water), but as soon as the ether is dry, it may be boiled with the sodium without further action. It now also gives no colour with picric acid.]

26. *Ether from Ethyl Bromide or Iodide*.—Dissolve 1 gram of sodium in 15 cc. absolute alcohol keeping cool; add 2 cc. ethyl halide, and warm gently in a reflux apparatus until the sodium halide ceases to increase. (Test.) Distil, and salt out ether with brine; note low b.p. and odour.

## CHAPTER V

27. *Oxidation of Alcohol to Acetic Acid*.—Dissolve 14 grams permanganate in 200 cc. water, in a litre flask with reflux condenser; add 8 cc. concentrated sulphuric acid, and then pour 5 cc. spirit in 50 cc. water slowly

down the condenser; the action must not become violent. When it is finished, boil for some time, and if the colour of the permanganate is discharged, add more acid and permanganate solution; finally, distil about three-fourths over. Note acidity to litmus and taste. Neutralise with soda, and evaporate as below. Apply qualitative tests.

30. *Acetic Acid from Vinegar*.—Distil vinegar. Note acidity of distillate. Neutralise with soda, and evaporate. Compare sodium salt with sodium acetate made from acetic acid as below. Apply qualitative tests.

29, 33. *Qualitative Tests for Acetic Acid*.—Distillable; acid reaction. Odour, with salts apparent on heating with dilute sulphuric acid. Ferric acetate, from ferric chloride and neutral acetate, red and soluble; hydrolysed (colour discharged) by dilute hydrochloric acid; hydrolysed to brown, insoluble basic salt by boiling with water, liquid becoming acid. Sodium acetate heated with dry white arsenic (very little of each) gives sickly odour of cacodyl oxide. Ethyl acetate; as with alcohol, § 19.

30. *Sodium Acetate*.—Exactly neutralise 100 cc. B.P. or 40 cc. glacial acid with washing soda, and boil down. When the solution begins to bump, stir vigorously until solid; then continue heating until the mass again fuses, and pour on a stone slab or the bottom of a retort stand. Note yield of sodium acetate (quantitative). Break up before quite cold, and keep in stoppered bottle.

30. *Glacial Acetic Acid*.—Distil 20 grams warm, recently-fused sodium acetate (above) in small lumps (not powder), with 20 cc. concentrated sulphuric acid; flask, condenser and receiver must be quite dry. Redistill from clean dry flask with 2 grams powdered sodium acetate, quite dry; note b.p., sp.gr., and m.p. If the acid will not freeze, after stirring vigorously, even in a freezing mixture of pounded ice and salt, add a crystal of pure acid frozen from stock.

30. *Melting Point*.—Best determined in large quantity in test tube (for small quantities, see § 49). If the substance is pure, the temperature remains constant as long as solid and liquid, well stirred, are present together. Jacket the test-tube with a somewhat larger empty tube.

30. *Pure Acetic Acid*.—Freeze 20 cc. glacial acid in test tube in ice, proceeding as directed until melting point ceases to rise; if the acetic acid contains no impurity besides water, its composition is given by the cryoscopic equation, § 14; about 1 per cent. of water for each 2° depression. Determine b.p. and sp.gr. of product. Note inflammability of warm acid.

[31. *Molecular Weight by Silver Method*.—Precipitate silver oxide with caustic soda from solution of 1 gram of silver nitrate in 10 cc. of water; wash free from alkali, and boil with dilute acetic acid; filter hot, and evaporate the acetate to dryness on a water-bath. Heat a weighed quantity to redness in a porcelain crucible, and weigh the residual frosted silver. Calculate molecular weight.]

## CHAPTER VI

33. *Copper and Lead Acetates*.—Dissolve the oxides or carbonates in boiling dilute acetic acid (compare §§ 31, 43); filter hot through a pleated filter (§ 25), crystallise and drain, and recrystallise from water, as from spirit (§ 25). To obtain large crystals, place a cold saturated solution in a



wide beaker or crystallising dish, add a crystal of the substance, cover the beaker with filter paper, and leave to evaporate spontaneously. Study hydrolysis of ferric acetate.

34. *Acetyl Chloride*.—Mix 20 cc. of glacial acid and 10 cc. of phosphorus trichloride in a flask, and pour into a narrow cylinder. When the upper layer ceases to increase, pour off carefully into a distilling-flask, using a funnel (direct distillation, without separation, does not give such good results). The whole of the apparatus must be *perfectly dry*. Note b.p. Yield 70 per cent. Keep in stoppered bottle—preferably capped. *Hydrolysis*.—Note action of water and caustic soda, and test for acetic and hydrochloric acids.

[35. *Acetic Anhydride*.—Add 10 cc. chloride to 16 grams recently fused, powdered sodium acetate as directed; when finished, remove a drop on a glass rod, and test with silver nitrate solution; distil when free from chlorine. Redistil and note b.p. It is best to redistil small quantities from a test-tube having a thermometer through the cork, and a short obtuse-angled tube to the condenser (as Fig. 5). Yield 70 per cent. Hydrolysis in same way as with chloride.]

36. *Reduction of Acetyl Chloride*.—To 5 cc. chloride in a loosely corked flask, add, over a day or two, 4 grams sodium in 7 cc. mercury. In making the sodium amalgam drop the sodium in small, freshly cut pieces into warm, dry mercury in a mortar, and press with a pestle; cover the mortar with a cloth, as the action is violent. The amalgam solidifies on cooling; keep in a stoppered bottle. When the reduction is finished, pour off from the mercury, which can be used any number of times, and boil gently (in reflux) with excess of 1 in 10 caustic soda; distil over a flame.

## CHAPTER VII

39. *Ethyl Acetate (Esterification of Acid)*.—Boil 2 cc. dry alcohol with 2 cc. glacial acetic acid in a test tube, and note changed odour.

Hydrogen chloride method: Pass the dry gas (§ 23) into one-fourth of a mixture of 20 cc. dry alcohol and 20 cc. glacial acetic acid, until saturated; mix with the remaining three-fourths, and boil in a reflux apparatus for two hours (on a water-bath); brine and sodium carbonate solution must be saturated; dry with solid potassium carbonate.

Continuous method: Heat 10 cc. spirit, 10 cc. glacial acetic acid, and 10 cc. concentrated sulphuric acid in a distilling flask on a water-bath, and when the distillation proceeds briskly, run in from a tap-funnel (stem to bottom of flask), at the same rate, a mixture of 50 cc. spirit with 50 cc. glacial acid. Purify by shaking repeatedly with small quantities of brine (ethyl acetate is soluble in 10 volumes of water).

Sodium acetate method: 50 grams acetate; 40 cc. each spirit and concentrated sulphuric acid, all in distilling flask; do not allow the temperature to rise. Cork and keep at least 24 hours; distil from water-bath without further treatment.

Note in each case b.p., sp.gr., and yield: 50–70 per cent.

40. *Hydrolysis of Ethyl Acetate*.—Boil 5 cc. acetate with 5 grams caustic soda in 10 cc. water (§ 22). Prove alcohol; acetic acid. The operation may be made quantitative by using a known volume of standard alcoholic potash, and a weighed amount of ester, titrating the alkali left at the end.

41. *Action of Acetyl Chloride and Acetic Anhydride on Alcohol.* Add a cc. acetyl chloride to 2 cc. dry alcohol; salt out and wash with saturated sodium carbonate. Try also with amyl alcohol (fusel oil); note pear odour. [Same with anhydride, but action is less violent; best by adding alternately a drop of anhydride and two or three drops of soda to the alcohol, shaking each time.]

## CHAPTER VIII

43. *Methyl Alcohol.*—Dehydrate 100 cc. of commercial methyl alcohol in the same way as ethyl alcohol (§5). Note b.p., sp.gr., inflammability presence of carbon and hydrogen. Make *sodium methoxide* in the same way as sodium ethoxide, but note there is no discoloration. Make *methyl acetate* from the alcohol, acetic acid and sulphuric acid in a test tube, and note the odour. Make *methyl potassium sulphate* in exactly the same way as the ethyl sodium salt, and with the same quantities. Yield 25 per cent. Keep in stoppered bottle for § 63. Make *methyl iodide*: To 10 cc. dry methyl alcohol in distilling flask, add (through paper shoot)  $2\frac{1}{2}$  grams red phosphorus and 25 grams iodine, *cooling when action is too vigorous*. Next day distil and purify as with ethyl iodide, § 20. Yield 80 per cent.

44. *Formic Acid.*—From methyl alcohol: Boil a little methyl alcohol in a distilling flask with acid permanganate, and pass the gas through lime water; distil, and test the distillate as below. From oxalic acid: 30 grams crystallised acid and 50 cc. glycerol as directed, *not above 135°* (thermometer bulb in mixture); test for carbon dioxide. At 135°, add 30 grams more oxalic acid, and again a third time; note odour and acidity of product, and conversion into carbon monoxide by concentrated sulphuric acid; test as below. Mix distillates and redistil; yield 40 cc.

44. *Barium Formate.*—Add excess barium carbonate to hot acid (25 cc. above, diluted, stirring well; boil until neutral, and filter; evaporate to crystallisation. Cover up for 24 hours; drain crystals, and dry on porous plate; evaporate mother liquor for second crop. Keep in a well corked tube. Convert 5 cc. of acid into *lead formate*, using litharge in same way, and 5 cc. into *copper formate*, using precipitated, washed copper oxide.

44. *Qualitative Tests for Formates.*—Acid reaction and odour, carbon monoxide evolved on heating with concentrated sulphuric acid (blue flame). Ferric formate as ferric acetate. Formates reduce ammonio-silver nitrate and acid mercuric chloride; acetates do not.

[44. *Synthesis of Formic Acid from Carbon Monoxide.*—Prepare pure carbon monoxide by dropping cold concentrated sulphuric acid from a tap-funnel on lumps of 98 per cent. potassium cyanide; wash the gas with 25 cc. 30 per cent. caustic soda, and dry with concentrated sulphuric acid. Pass the pure gas through a small U-tube filled with ordinary soda lime, and immersed in an oil-bath (melted paraffin wax in an enamelled iron pot) at 180–200°. Note that comparatively little escapes, until after an hour.

Cool the U-tube, powder its contents, mix with much water, and acidify strongly with dilute sulphuric acid. Filter at the pump (§ 25) from calcium sulphate, and distil the clear filtrate as long as acid passes over, keeping the level constant by adding water from time to time. Neutralise the distillate with sodium carbonate, and evaporate to dryness on a water-bath. The residue is sodium formate; test.]

45. *Butyric and Caproic Acids*.—Melt 25 grams of butter in a beaker in a water-bath, and filter through a hot, dry filter (under a hot sand-bath). Heat the filtered fat with 60 cc. spirit and 10 grams caustic soda on a water-bath, until a clear yellow solution is obtained; expel the alcohol by adding water, heating on the water-bath until the odour and colour change. After distilling with sulphuric acid, note the acidity and rancid odour of the distillate; neutralise with sodium carbonate, add calcium chloride, and boil; calcium butyrate is precipitated; collect hot. About one-third of the acid is caproic acid; it distills with steam more rapidly than the butyric acid.

[45. *Synthesis of Propionic Acid*.—Dissolve 2 grams bright magnesium turnings in a solution of 7 cc. dry ethyl iodide in 10 cc. dry ether (dried over sodium and redistilled, § 26) in a small reflux apparatus (moderate the action by cooling, if necessary); and pass in carbon dioxide (wash with sodium carbonate solution, and dry twice with concentrated sulphuric acid) until it ceases to be absorbed; cool, if necessary. Distil the ether from a water-bath, and boil the residue with excess of dilute sulphuric acid (adding water as necessary) as long as volatile acid distills. Convert the distillate partly into sodium salt, and partly into silver salt: test the former (as acetate, but very deliquescent) and analyse the latter (§ 31). Yield 50 per cent. Compare § 267.]

46. *The Ethereal Salts*.—Warm some calcium butyrate with a little dry alcohol and concentrated sulphuric acid, and note pineapple odour of ethyl butyrate. For amyl acetate see § 41. [From commercial butyric acid, make methyl butyrate by continuous esterification process (§ 39), using half quantities given for acetates; b.p. 102°.]

## CHAPTER IX

48. *Saponification of Fat*.—Boil 10 grams of clarified suet with a solution of 10 grams of caustic soda in 50 cc. of water; maintain level of liquid carefully, and boil vigorously. (Or pour melted fat into 15 cc. spirit, shaking vigorously, and add cautiously to the granulated mass, a hot solution of the soda in 10 cc. of water, again shaking vigorously; when the action is over, mix the product with 200 cc. of water and boil gently, adding water from time to time, until the alcohol is expelled). Salt out, purify and dry soap, and test detergent properties.

48. *Hydrolysis of Soap*.—Add a few drops of phenol-phthalein solution to a concentrated aqueous solution of soap, and just neutralise with very dilute sulphuric acid. On dilution with water the solution becomes alkaline.

49. *Fatty Acids*.—Proceed as directed: 5 grams soap in 50 cc. hot water; excess of dilute sulphuric acid; after washing the cake of acids by repeatedly melting with water, recrystallise from hot alcohol (§ 25). Note faint acid reaction. Dissolve in hot caustic soda, avoiding excess; add calcium chloride and magnesium sulphate to portions of solution, and note curdy precipitates as with hard water; note also insoluble lead soap with lead acetate.

49. *Melting Point of Small Quantities*.—For small quantities, the capillary tube method is the best. Ordinary  $\frac{1}{4}$  inch soft glass tubing 3 in. long

(or a small test-tube) is drawn out at the middle to a 2 mm. capillary, and then fused into two tubes, the capillary portion of which (4 cm. long) should take a large pin. Fill 5 mm. of the capillary with powdered solid, and fasten it to the thermometer stem with a band cut from rubber tube, so that it rests against the bulb, but the open end against the stem (Fig. 12); if the bulb of the thermometer is of the same diameter as the stem, the capillary adheres to it by surface tension, and the band is unnecessary. Immerse the bulb and lower part of capillary (not the upper part) in the small beaker of water or sulphuric acid, at a temperature below the melting point of the substance; stir well, and warm gradually. If the substance is pure, the opaque solid suddenly changes to a transparent liquid on reaching its melting point; and conversely the liquid is as suddenly reconverted into the solid on cooling to its freezing point. The melting and freezing points are then practically identical; if they extend over several degrees, the substance is impure.

Another very convenient method is to fit the thermometer (with the capillary, as before) through a cork to a small test-tube, holding enough sulphuric acid to cover the bulb; this test-tube is slipped into a small flask, containing sulphuric acid to the same level. Stirring is then easily effected by giving a gentle rotatory motion to the flask. If the sulphuric acid darkens, from charred dust, etc., add a small crystal of nitre.

## CHAPTER X

53. *Acetamide*.—Keep 20 cc. ethyl acetate (or 25 cc. of crude distillate from the continuous process, § 39), with 20 cc. strongest ammonia, sp.gr. 0.880, in a corked flask, until homogeneous (24–48 hours); the flask should be kept in a warm place in winter, or the action will be very slow. Identify alcohol in the early distillate (acidify and redistil). Recrystallise product until m.p. is constant. Note b.p. Yield, 50 per cent.

54. *Detection of Nitrogen*.—Heat a crystal of acetamide with soda-lime, and note ammonia. Heat with sodium to redness in small tube for at least half a minute; break hot in 5 cc. water; filter. Add a few drops of ferrous sulphate and ferric chloride and some caustic soda; warm, acidify with dilute hydrochloric acid—Prussian blue.

[54. *Estimation of Nitrogen by Combustion or Absolute Method*.—Combustion tube, 75 cm. long, 1.5 cm. internal diameter, closed at one end. To fill the tube, clamp in vertical position, and introduce in order, through a wide-necked funnel: (a) 10 cm. sodium hydrogen carbonate (*free from ammonia*) followed by a 1 cm. copper gauze roll, superficially oxidised in flame; (b) 7 cm. coarsely granulated or “wire” copper oxide (a stock of this is heated to dull redness in a furnace, and kept in a well-corked flask) followed by a similar oxidised roll; (c) a mixture of weighed quantity of powdered substance with enough powdered copper oxide (a stock of this heated and kept as above) to fill 6 cm. of the tube (to mix, place oxide in a small, dry flask, add substance from weighing tube, cork, and shake well), followed by 2 cm. powdered oxide (to rinse out flask), and a 1 cm. copper roll; (d) 24 cm. granulated or “wire” copper oxide; (e) roll of copper gauze, 12 cm. long, wound on stout copper wire bent into a hook at

each end (the roll is reduced by dropping red-hot into a test-tube containing a little methyl alcohol); (f) 10 cm. empty.

Place tube horizontally, and tap, to make a channel for the gases; introduce into furnace (5 cm. projecting) and connect to nitrometer, previously filled with 50 per cent. potash (not soda; 200 grams potash to 200 cc. water); enough mercury to cover the gas inlet (the rubber joint should be very short, and the rubber cork of the combustion tube should fit well, and be protected from the heat by an asbestos screen—Fig. 13). The potash reservoir having been lowered, and the tap opened, a single burner is lit under the end of the sodium bicarbonate, to generate carbon dioxide; then 5 minutes later, the burner under the copper roll. After the current of carbon dioxide has passed for 10 minutes the air should be practically expelled; test by raising the potash reservoir and closing the tap. If only very minute bubbles rise to the surface (these never quite cease), light the burners under the layer of copper oxide next the bicarbonate, and after finally adjusting the nitrometer, cautiously heat the part of the tube containing the substance, lighting one burner at a time. When gas ceases to collect in the nitrometer, and the whole of the tube (except the bicarbonate) is at a dull red heat, heat the rest of the bicarbonate gently, until again only minute bubbles of gas rise to the surface of the potash. Then disconnect, leave for an hour in a place of uniform temperature, and measure the nitrogen; noting the temperature and barometric pressure. The gas may be measured in the nitrometer, levelling by means of the potash reservoir (the vapour pressure of 50 per cent. is roughly 25 per cent. of that of water at the same temperature—see § 12); or by attaching a short-necked funnel to the upper tube, and filling this with water, it may be transferred to another measuring tube, and measured over water (for vapour pressure, see § 12). The whole operation should not occupy more than 2 hours.]

[54. *Estimation of Nitrogen by Sulphuric Acid Method (Kjeldahl).*—The substance (0.5 gram) is heated in a round bottomed flask on a sand-bath, with cc. concentrated sulphuric acid (*free from nitrogen*), just short of boiling, and when dissolved, powdered permanganate is added in very small quantities until the liquid is permanently coloured green or purple. The nitrogen is thus converted into ammonium sulphate, and the carbon completely oxidised. The cooled solution is cautiously mixed in the same flask with 150 cc. of cold water, a little powdered talc is added, to prevent bumping, and 50 cc. of 50 per cent. caustic soda is cautiously run into the flask, so that it passes under the acid without mixing. The flask is now fitted with a bulb distillation tube ("Kjeldahl trap"), shaken to mix the soda, and then briskly distilled for 20 minutes, the ammonia being received in decinormal sulphuric acid. The excess of acid is then titrated with decinormal alkali.]

[54. *Estimation of Carbon and Hydrogen in Nitrogenous Substances.*—Use silver roll as in halogen carbon estimation (§§ 21, 25), or copper as in nitrogen estimation.]

55. *Hydrolysis of Acetamide.*—Boil 1 gram in open flask with 2 grams caustic soda in 20 cc. water, and note ammonia; when this has disappeared distil with excess of dilute sulphuric acid, and test distillate for acetic acid. Action of nitrous acid: 1 gram in 10 cc. water and excess of dilute sulphuric acid; solution of 1 gram of nitrite in 10 cc. water added until paper is blue. Potassium-iodide-starch papers: rub  $\frac{1}{2}$  gram starch with 20 cc. cold water, boil and cool; add  $\frac{1}{2}$  gram iodide; dip strips of filter paper,

and dry in air. After adding the nitrite, prove that the escaping gas is nitrogen, and then distil the residue for acetic acid.

56. *Acetonitrile*.—Acetamide, pure or crude, 5 grams; redistil nitrile from water-bath with (a) moist and (b) dry potassium carbonate. Note b.p., yield (4 cc. = 90 per cent.), odour, and colour of flame.

56. *Hydrolysis of Acetonitrile*.—Boil 2 cc. nitrile with 5 grams caustic soda in 25 cc. water (§ 22). Prove ammonia and acetic acid as directed.

57, 58. *Ethylamine*. Add by degrees 5 grams zinc to 2 cc. nitrile in 50 cc. water with 5 cc. concentrated hydrochloric acid. Next day, add excess of caustic soda (10 grams in 50 cc. water), and distil; the end of the condenser tube should dip under a little water in receiver. Note odour and alkalinity of distillate. Neutralise with dilute hydrochloric acid, and evaporate to dryness; warm evaporated residue with dry alcohol on a water-bath; filter, and evaporate filtrate to dryness on water-bath. Heat some of the residue with soda-lime as in making ammonia, and note odour, alkalinity and inflammability of gas (test for carbon dioxide).

## CHAPTER XI

61. *Formonitrile* (dilute).—Distil 5 grams 98 per cent. potassium cyanide with 50 cc. dilute sulphuric acid (1 vol. in 10); this must be done in a good draught cupboard, as *prussic acid vapour is extremely poisonous*. Note cyanide tests (§§ 54, 201).

62. *Synthesis of Formic Acid*.—Potassium cyanide, 4 grams, with 5 grams caustic soda and 50 cc. water (§ 22); eliminate unchanged cyanide as directed (work in draught cupboard). Prove formic acid and ammonia.

62. *Synthesis of Methylamine*.—To distillate from § 61 add 50 cc. water and 5 cc. concentrated hydrochloric acid, and, then, gradually (as with acetonitrile) 5 grams granulated zinc. Keep in loosely corked flask; next day remove excess of zinc, and boil vigorously (*in draught cupboard*) until remainder of prussic acid has disappeared; then proceed as with ethylamine. Note practical identity in properties.

63. *Synthesis of Acetic Acid*.—Dry methyl sodium sulphate, 10 grams, and 5 grams dry 98 per cent. potassium cyanide, finely powdered *and intimately mixed*; distil from test tube (or small flask) connected with condenser, heating *cautiously*. Shake the distillate with 1 cc. dilute sulphuric acid (to destroy unpleasant isocyanide), then boil in reflux apparatus with 10 grams caustic soda in 50 cc. water until evolution of ammonia partially ceases. Well acidify with dilute sulphuric acid, boil with  $\frac{1}{2}$  gram mercuric oxide, and distil. Prove distillate is acetic acid: reaction, odour and tests. Yield 30 per cent. [Convert some of the distillate into the silver salt, and analyse (§ 31).]

64. *Synthesis of Propionic Acid*.—As with acetic acid, but using ethyl sodium sulphate. Test as in § 45.

## CHAPTER XIII

72. *Methane from Acetic Acid*.—Finely powder 5 grams recently fused sodium acetate (§ 30), 6 grams soda-lime, and *intimately mix* with 5 grams clean iron filings. Heat in hard glass tube with delivery tube, with a roll of filter paper in front to absorb moisture; heat from back to front, the tube being inclined towards the front. Note the gas, colourless, insoluble, light; burns to carbon dioxide. Does not decolorise bromine water or cold alkaline permanganate (diluted until transparent and mixed with a few drops of sodium carbonate solution).

[72. *Methane from Magnesium Methiodide*.—Dissolve  $1\frac{1}{2}$  grams bright magnesium turnings in a solution of 5 cc. dry methyl iodide in 7 cc. dry ether (see § 45) in a small flask fitted with tap-funnel and gas delivery tube. When the action is finished, distil off the ether on a water-bath, and drop the water slowly on the residue. Wash the gas well with water to eliminate ether vapour, and test as above.]

73. *Chloroform*.—The bleaching powder (150 grams) is made into a thin cream with 500 cc., water, and 20 cc. spirit or acetone, diluted with twice its volume of water, is added; distil with steam at once. Chloroform is rather soluble in water, hence add brine to distillate. Purify. Note odour, b.p., sp.gr. Yield 75 per cent. with acetone (much less with alcohol). No precipitate with silver nitrate when pure.

73. *Qualitative Tests for Chloroform*.—Volatility. Odour. Formation of chloride with alcoholic soda (blank experiment should be made, as soda is liable to contain chlorides). Reduces alkaline copper tartrate (§ 159) on boiling. Warm with alcoholic soda and a drop of aniline in test tube; characteristic odour of phenyl isocyanide.

74. *Iodoform*.—Add 4 cc. spirit or acetone to solution of 10 grams washing soda in 50 cc. water. Warm to  $70^{\circ}$ , and add iodine (about 5 grams) until slight brown colour remains; then 1 drop caustic soda, when colour should change to yellow. Purify as directed. Note odour, hexagonal crystals (under lens); m.p. by capillary tube method. Yield quantitative.

75. *Hydrolysis of Chloroform and Iodoform*.—Chloroform, 5 cc.; soda, 5 grams; spirit, 50 cc. Boil in reflux apparatus, and when odour has disappeared distil off the alcohol on a water-bath. Prove that the residue contains chloride and formate. Iodoform, similarly, but without reflux apparatus.

## CHAPTER XIV

77. *Ethane, by Reduction*.—A very small flask, fitted with a cork and delivery tube, is filled with granulated zinc, which is cleaned by covering with dilute sulphuric acid until action has set in; it is then washed with water, and coated with copper by covering with a very dilute solution of copper sulphate (1 gram in 100 cc.). When the zinc is black with reduced copper it is again washed with water, and the flask filled up with spirit, containing 10 cc. of ethyl bromide (or iodide); gas is slowly evolved, and is collected during the night in a large jar or flask over water. Next day the accumulated gas is decanted into smaller vessels, and examined as with methane (§ 72).

[79. *Purification and Properties of Light Petroleum*.—Purify 50 cc. of "benzoline" (from oil-shop) by shaking successively with strong soda, concentrated sulphuric acid, and water; dry with calcium chloride, and fractionate carefully (the vapour is heavy and *very inflammable*). Prove that there is no action with concentrated sulphuric or nitric acids, bromine water or alkaline permanganate.]

## CHAPTER XV

82. *Preparation of Crude Aldehyde*.—From alcohol: Run a cold mixture of 45 cc. spirit, 120 cc. water, and 22 cc. concentrated sulphuric acid slowly, from a tap funnel, into a distilling flask containing 30 grams bichromate (small crystals, not powder), cooling if necessary. Afterwards heat on water-bath, *but not with flame*. Redistil distillate, noting odour and b.p.

[82. *Preparation of Aldehyde-Ammonia and Pure Aldehyde*.—Large flask (Fig. 16) with 100 grams potassium dichromate in large crystals (or 90 grams sodium dichromate in 200 cc. of water—in which case only 200 cc. of water with the alcohol and acid). Run in from a tap funnel, drop by drop, a mixture of 150 cc. spirit, 400 cc. water, and 72 cc. concentrated sulphuric acid; cooling with water if action is too vigorous. The reflux condenser is supplied with warm water (about 30°), best by passing condenser water to bottom of a small flask (not shown in photograph) heated in a water-bath; the temperature is given by a thermometer just through the cork of the flask—the slower the current of water, the higher the temperature. The Volhard trap is made from two gas cylinders (or large boiling tubes) with well-fitting corks, and the connections must be wide, to prevent choking by crystals.

The ammonia gas is obtained by heating .880 ammonia in the middle flask, and is dried over quicklime. The ether (50 cc.) must be dried for two days over calcium chloride, and poured off before use. When ammonia passes freely through the ether, pour the liquid off, and scrape the aldehyde-ammonia out on a porous plate. Yield 25–30 per cent.

Dissolve the aldehyde-ammonia (20 grams) in 20 cc. ice-cold water, and add ice-cold, dilute sulphuric acid until distinctly (but not strongly) acid. Then warm cautiously on water-bath, dry vapour with warm calcium chloride (U-tubes in beaker at 40–50°), and condense at 0° (an ordinary condenser may be used, the cooling water first passing, slowly, through a bottle packed with ice). Yield 80 per cent.

83. *Qualitative Tests for Aldehyde*.—Odour. Silver reduction (§ 44). Reduces alkaline copper tartrate (§ 159). Rosaniline test; one drop of dye solution only, much sulphurous acid. Aldehyde resin. Phenylhydrazine: 3 drops of phenylhydrazine in 3 drops of glacial acetic acid; add 5 cc. of water, and filter if necessary before adding the aldehyde.

83. *Reduction of Acetic Acid to Aldehyde*.—Acetyl chloride and sodium amalgam as before (§ 36), but stop after an hour, acidify and distil. Test distillate as above. Barium formate method: Acetate from 50 cc. B.P. or 20 cc. glacial acid in same way as formate (§ 44); 5 grams formate; 8 grams acetate; mix as described. Distil as Fig. 17, § 88, heating from behind; the tube should slope downwards towards the mouth. Collect distillate in a little water. Filter and test.



83. *Oxidation of Aldehyde to Acetic Acid*.—Add 5 cc. aldehyde in 50 cc. water to acid permanganate, in a reflux apparatus, precisely as with alcohol (§ 27), but cautiously, as the action is violent. Test the distillate for acetic acid.

83. *Reduction of Aldehyde to Alcohol*.—Add gradually 50 grams 4 per cent. sodium amalgam (§ 36) to 5 cc. aldehyde in 50 cc. water, keeping solution always *distinctly acid* with dilute sulphuric acid, or aldehyde will be resinified. When the odour of aldehyde has disappeared, pour from the mercury, distil, and test for alcohol.

[85. *Paraldehyde and Metaldehyde*.—From pure aldehyde in manner described. Metaldehyde also from crude aldehyde and calcium chloride—24 hours. Pure aldehyde may be made by boiling commercial paraldehyde with a small quantity of concentrated sulphuric acid in a reflux apparatus, with condenser at 50° (§ 82) to return any unchanged paraldehyde.]

86. *Formaldehyde*.—Fit a 3-inch length of combustion tube with corks and leading tubes, introduce a 2-inch roll of copper gauze, and connect (a) to filter pump, through a small wash-bottle, cooled in water (*short* tube to pump); (b) to *short* tube of small wash-bottle, immersed in vessel of water at 40°, and containing 20 cc. of methyl alcohol (inlet tube for air beneath alcohol). Heat copper roll to *dull* redness, and set pump going. Test dilute formaldehyde which collects in flask. All tests as with acetaldehyde (but no resin); neutralises ammonia. Add a few drops to some milk (or fragment of cheese ground up with water), and then concentrated sulphuric acid to form a lower layer; a violet ring is formed at the junction.

86. *Oenanthaldehyde*.—Distil 5 cc. of castor oil briskly from a test-tube; shake crude distillate with dilute soda, separate upper layer, and examine by aldehyde tests.

## CHAPTER XVI

88. *Acetone*.—Powder 50 grams barium acetate, and dry in porcelain dish on sand-bath; distil in 4 portions. Shake crude distillate with twice its volume of bisulphite solution (a greenish liquid, made by saturating warm water with sodium metabisulphite). Dry crystals on plate, and then as described. *Qualitative tests* on dilute liquid (or salt out with calcium chloride): hydrazone as aldehyde, but no resin, silver or rosaniline if pure; chloroform (odour) with bleaching powder.

[89. *Acetoxime*.—To a solution of 3 grams hydroxylamine hydrochloride in 5 cc. water add 1½ grams of dry sodium carbonate dissolved in 10 cc. water, and then 4 cc. of acetone; cork and leave over night. Next day shake in a tap-funnel with 20 cc. ether, pour off the ethereal solution of acetoxime, and repeat with another 20 cc. Filter the combined extracts through a small filter (wetted with ether), and evaporate the ether in a small dish over warm water (no flame). Transfer the residue to a watch-glass, keep melted on a water-bath until free from ether and water, and allow to crystallise. Take m.p. Yield 70 per cent. Warm a small portion of acetoxime with alkaline copper tartrate (§ 168); there is no reduction (if free from hydroxylamine). Dissolve another portion in a little concentrated hydrochloric acid, and evaporate to dryness on a water-bath; the residue (hydroxylamine hydrochloride) now reduces Fehling's solution.]

90. *Oxidation of Acetone*.—Add gradually through reflux condenser 5 cc. acetone in 50 cc. water, to solution of 12 grams permanganate in 100 cc. water, acidified with 10 cc. concentrated sulphuric acid. Prove carbon dioxide. Distil when permanganate is no longer decolorised on boiling, and test for acetic acid.

91. *Zinc Methyl*.—Dry reflux apparatus; small U-tube at top with drop of mercury in bend. In flask, intimate mixture of 15 grams zinc dust and 5 grams reduced copper; add 15 cc. methyl iodide and proceed as directed; dry the carbon dioxide (§ 45). (Reduce copper as in § 260, but dry on porous plate, and finally at 100°.) The zinc methyl must be received in tubes drawn out at the neck (condenser end being also drawn out), and sealed immediately.]

92. *Isopropyl Alcohol*.—Acetone (10 cc.) with sodium amalgam, exactly as with aldehyde. Renew mercury as it becomes liquid; repeated treatment with the amalgam is required (altogether 25 cc. of mercury, with 14 grams of sodium). When hydrogen at last comes off freely, pour off and distil; finally, salt out and dry with solid caustic soda. Note b.p., and action of sodium and acetyl chloride. Isopropyl acetate, fruity odour.

93. *Isopropyl Iodide*.—Glycerol 16 cc., water 16 cc., iodine 28 grams; mix well in distilling flask, warming if necessary; cool, add slowly 5 grams yellow phosphorus in small pieces (need not be dry), replacing cork at once (no thermometer). When all the phosphorus is added, return distillate to flask, and redistil to dryness from a water-bath; repeat this three times. Then purify as with ethyl bromide (§ 20) and redistil for boiling-point. Yield 30-35 per cent.]

## CHAPTER XVII

[97. *Isobutyl Alcohol*.—Boil 2 cc. commercial isobutyl alcohol in a reflux apparatus in a sand-bath, with 20 grams dichromate and 20 cc. concentrated sulphuric acid in 200 cc. water; small fragments of porous earthenware must be added to stop bumping. Pass the evolved carbon dioxide through a Volhard trap (Fig. 18, § 114) containing lime-water, and note the relatively enormous quantity. When the evolution of gas ceases, distil; dilute distillate to 500 cc. and again distil briskly. Any unoxidised isobutaldehyde and isobutyric acid pass over in the early portions (test); neutralise the later distillate with sodium carbonate, boil down to dryness, and prove residue is sodium acetate. Analyse silver salt.]

[98. *Tertiary Butyl Alcohol*.—Dissolve 4 grams of bright magnesium turnings in a solution of 10 cc. of dry methyl iodide in 10 cc. dry ether (as in § 45); moderate the action by cooling the distilling flask, as it is very vigorous. When the metal has nearly dissolved (there should be a slight excess), cool well, and add cautiously 12 cc. of dry acetone. When the action is again finished, distil off the ether (water-bath), acidify the residue with dilute sulphuric acid, and distil. The tertiary butyl alcohol floats on the water (salt out the dissolved portion with caustic soda, and separate the upper layer); dry with solid soda; redistil; crystallise by cooling in ice or ice and salt, if necessary. Yield 40-50 per cent. Try action of acetyl chloride.]

## CHAPTER XIX

103. *Ethylene*.—To prepare sample of gas, heat 10 cc. spirit with 30 cc. sulphuric acid in a distilling flask at  $180^{\circ}$  (*thermometer in liquid*); wash with caustic soda, and collect over water. Note odour, taste. Luminous flame. Instantly decolorises bromine water, and dilute alkaline permanganate (§ 72). From ethyl bromide: 5 cc. bromide in test tube, connected with 6 in. length of hard glass tube containing 3 in. soda-lime; packed with asbestos at each end; heat to redness with one burner; boil bromide *gently*, and collect evolved gas. Wash and test as before; test residual soda-lime for bromide.

104. *Ethylene Bromide*.—Ethylene from alcohol and 50 cc. syrupy phosphoric acid, as described, running in alcohol *beneath the surface of the liquid*, as in making ether; the thermometer bulb must be beneath the surface. Pass gas through (1) water, and (2) concentrated sulphuric acid, into large flask containing 10 cc. bromine and 10 cc. water. Purify as described. Note odour, b.p., m.p., and sp.gr. Yield 90 per cent.

106. *Olefines in Coal Gas*.—Pass coal-gas into small flasks containing bromine water and dilute alkaline permanganate (§ 72); note decolorisation.

## CHAPTER XX

109, 110. *Acetylene*.—From 3 cc. ethylene bromide and soda-lime in same way as ethylene. Odour; smoky flame; silver and copper compounds. Silver: 0.5 gram nitrate in 5 cc. water, acid ammonia until precipitate just redissolves; use 2 cc. Copper: 5 grams turnings and 5 grams copper oxide, boiled with 20 cc. concentrated hydrochloric acid until a brown, syrupy solution is obtained. Pour off into some cold, recently boiled, distilled water, allow precipitated cuprous chloride to settle, and dissolve in 25 cc. cold saturated ammonium chloride; keep in stoppered bottle, full to stopper and containing some copper turnings. Use 5 cc. with enough ammonia to redissolve initial precipitate. From Bunsen flame: strike back, and test with small inverted flasks moistened with the metallic solutions. From calcium carbide: fragment under beaker at pneumatic trough, *quickly*, with tongs; or, for larger quantity, place carbide in small flask, with delivery tube, and drop water *cautiously* from a tap-funnel (take care that all air is expelled, before collecting). Examine gas as before.

## PART II

### CHAPTER XXI

[114. *Chloracetic Acid*.—Boil 100 cc. glacial acid gently with 10 grams flowers of sulphur, with reflux, in bright daylight (direct sunlight if possible), and pass chlorine in until a few drops of the product crystallise at 0° (6 to 12 hours, according to light). Fractionate; above 180° crystallises; drain quickly, because hygroscopic; take melting-point. Yield 50 per cent. Acid is very corrosive.]

[114. *Bromacetic Acid*.—Heat 40 cc. glacial acetic acid with 10 cc. acetyl chloride (crude, poured off phosphorous acid, § 34), 2 hours in reflux apparatus on water-bath. Cool; add 50 cc. bromine; attach trap (100 cc. water), and heat 1 hour on water-bath. When bromine has disappeared, distil product, and as soon as distillate freezes readily, collect apart, and drain crystals. Determine melting-point; test for halogen. Bromacetic acid is very corrosive. Yield 80 per cent.]

[114. *Trichloracetic Acid*.—Warm 10 grams chloral hydrate with 8 cc. red nitric acid (sp.gr. 1.5) in flask (draught) until action starts, and finally boil gently to complete action. Fractionate (as with acetamide, § 53, no condenser at final stage), collect 180–200°; crystallise; take melting-point. Yield 50 per cent. Prove hydrolysis to chloroform and carbonate on 1 gram.]

115. *Chloral Hydrate*.—Hydrolyse 1 gram with cold soda; filter from chloroform (which prove), boil briskly, and test for formate. Reduces ammoniacal silver quickly, and alkaline copper tartrate (§ 159). Reduce 1 gram in water with sodium amalgam in same way as aldehyde; after two or three days pour off, distil and test for alcohol.

115. *Qualitative Tests for Chloral Hydrate*.—Volatile with steam. Odour. Hydrolysis. Reduces ammoniacal silver and alkaline copper tartrate. Phenyl isocyanide as with chloroform. Gives reddish-brown precipitate with ammonium sulphide, especially on warming.

115. *Chloral*.—Cover 2 grams chloral hydrate with concentrated sulphuric acid in a test-tube, and warm gently. Liquid chloral floats. Remove with fine pipette, and add 1 drop of water; heat is evolved, and the hydrate is re-formed.

### CHAPTER XXII

[119. *Glycollic Acid*.—A fair yield by boiling potassium chloracetate or bromacetate solution (*exactly* neutralised) with reflux for several hours. Potassium chloride separates on concentration; evaporate remaining

solution to dryness, and extract acid with hot acetone. Note acid reaction of solution; evaporate.]

119. *Glycollic Acid*.—Dissolve 10 grams powdered 98 per cent. potassium cyanide in 50 cc. water, and add 13 cc. 40 per cent. formaldehyde, warming (not above 30°) until dissolved; leave for an hour, and then add slowly (in draught) cold, dilute hydrochloric acid (32 cc. concentrated acid in 50 cc. water), stirring well. Boil to expel any prussic acid, and evaporate to dryness on water-bath. Powder residue, and boil in reflux apparatus with 25 cc. acetone; evaporate filtered extract (note acid reaction). Distil some crystals of glycollic acid with concentrated sulphuric acid; note carbon dioxide and sublimate of paraformaldehyde. Oxidise some crystals with nitric acid; evaporate to dryness and test for oxalic acid.

[120. *Glycol*.—Boil 10 cc. ethylene dibromide, 16 grams dry potassium carbonate, 150 cc. water, in reflux apparatus for 2 hours; or until bromide has disappeared; distil with steam (Fig. 21, § 244) and evaporate. Note sweet taste, and oxidation to oxalic acid.]

121. *Glyoxylic Acid*.—To 10 cc. saturated solution of oxalic acid, add enough sodium amalgam to fill one-third of the test-tube. After an hour pour off from the mercury, and neutralise exactly. Apply aldehyde tests (silver, rosaniline, phenylhydrazine acetate); add a few drops to some white of egg solution, followed by concentrated sulphuric acid—violet ring.

[121. *Glycollic Aldehyde*.—Dissolve a crystal of ferrous sulphate in a solution of glycol (cold), and add an equal bulk of hydrogen peroxide solution. Shake brown product with precipitated barium carbonate, and filter. Test colourless solution by aldehyde tests.]

122. *Oxalic Acid from Sugar*.—Add 100 cc. concentrated nitric acid to 25 grams cane sugar in 130 cc. water, and warm (very heavy fumes). Recrystallise from small quantities of water until free from nitric acid. Note acid reaction, and loss of water at 100°. Test tube in beaker of boiling water; with current of dry air, drawn first through calcium chloride; note sublimed crystals.

122. *Qualitative Tests for Oxalates*.—Calcium salt (calcium chloride to neutral oxalate) insoluble in water and boiling acetic acid; heated gently on platinum foil leaves a residue of calcium carbonate, which effervesces with acids. With concentrated sulphuric acid, gives carbon monoxide and dioxide. With warm acid permanganate, carbon dioxide is evolved, and permanganate decolorised.

123. *Ammonium Oxalates*.—Solution of 20 grams acid into two equal parts. First exactly neutralised with ammonia, and evaporated to crystallisation—normal oxalate. Second again divided; half neutralised, mixed with remainder, and evaporated as before—acid oxalate; note different shape of crystals and acidity to litmus.

123. *Ethyl Oxalate*.—Crystallised oxalic acid (40 grams) is dehydrated in a flask as above (§ 122) until there is no further loss of weight (11½ grams loss). Heat with 25 cc. dry alcohol as directed (thermometer in liquid), passing in vapour of 33 cc. more as in steam distillation. Fractionate; note b.p. and sp.gr. Use the distilled alcohol for oxamide (below). Hydrolysis as usual (§ 40); prove alcohol and sodium oxalate.

124. *Oxamide*.—Ammonia to distilled alcohol from ethyl oxalate preparation; also to 1 cc. of pure ethyl oxalate. Wash precipitate, dry and filter. Hydrolysis in test tube; prove ammonia and oxalate. Nitrous acid, as acetamide (§ 55).

[124. *Oxalonitrile*.—Heat  $\frac{1}{2}$  gram of oxamide with a little phosphorus pentoxide in small bulb tube, and note pink flame of cyanogen (*very poisonous*). Dissolve yellow mercuric oxide in hot dilute prussic acid, evaporate the clear solution, and crystallise and drain mercuric cyanide. Heat dry crystals in small bulb-tube and again note pink flame.

[124. *Oxamide from Cyanogen*.—Dissolve 25 grams crystallised copper sulphate in 75 cc. water in a distilling flask (water-bath), and add slowly from a tap-funnel a warm solution of 12 grams 98 per cent. potassium cyanide in 25 cc. water (*draught cupboard; cyanogen gas is extremely poisonous*). Pass the evolved cyanogen into 20 cc. cold concentrated hydrochloric acid, and when all the cyanide has been added, expel the second equivalent of cyanogen by adding, in the same way, a solution of 16 grams of ferric chloride in 20 cc. water. If the hydrochloric acid is kept cool, there will now be a copious crystalline precipitate of oxamide. Collect on a filter, wash with water, and dry; test by hydrolysis to sodium oxalate (test) and ammonia.]

## CHAPTER XXIII

127. *Glycerol*.—Saponify fat with aqueous soda (§ 48), and distil clear lye with steam (§ 244). Evaporate on water-bath, and test syrupy residue for glycerol, comparing with stock. *Qualitative Tests*.—Syrupy; sweet; leaves syrup on water-bath. Boiled to dryness with large excess of dry potassium hydrogen sulphate, turns brown and gives pungent acrolein, which collected in water reduces silver, resinifies with soda, and gives rosaniline test. Dry glycerol interacts vigorously with acetyl chloride (warm); benzoate with benzoyl chloride (§ 270).

129. *Glycerose*.—Mix 5 cc. glycerol with 5 cc. water, and add solution of  $\frac{1}{2}$  gram crystallised ferrous sulphate in 5 cc. water. Add slowly 20 cc. of 20 volume hydrogen peroxide (or more of weaker), *keeping cool*. When cold, shake with excess of precipitated barium carbonate, and filter. Boil off water from clear filtrate under diminished pressure (Fig. 20), not above 50°. Residue sweet; gives silver, rosaniline and phenylhydrazine tests (compare § 183).

[129. *Glyceric Acid*.—Mix 30 cc. glycerol with 38 cc. water; add, through long funnel, 26 cc. red nitric acid, sp.gr. 1.5, and proceed as directed.]

## CHAPTER XXIV

131. *Allyl Alcohol*.—Heat 20 grams oxalic acid with 30 cc. glycerol, and  $\frac{1}{2}$  gram ammonium chloride; collect formic acid apart; and stop at 260° (thermometer in liquid). Note b.p., sp.gr., action of acetyl chloride (fragrant acetate), bromine water and alkaline permanganate (§ 72). Oxidise a little to acrolein by distillation with chromic acid mixture, and test acrolein (§ 132).

[131. *Allyl Iodide*.—Add 25 grams iodine to 30 cc. dry glycerol (dried by heating at 175°) in distilling flask; dioxide washed with sodium bicarbonate solution, dried with sulphuric acid; tube into flask through ordinary

cork, no thermometer. Add 8 grams yellow phosphorus in small pieces; weigh in water, dry each piece quickly with filter paper, remove cork, and replace at once after each addition of phosphorus, warming to start action. Yield 65 per cent. *Hydrolysis*.—Boil 1 cc. with water in a reflux apparatus, and test with water for hydriodic acid.]

132. *Acrolein*.—Distil 5 grams glycerol with 10 grams potassium hydrogen sulphate, from test tube with bent tube to condenser. Dissolve crude product in water and filter. Note odour, silver, rosaniline, resin and action of bromine water.

[132. *Acrylic Acid*.—From 1 cc. acrolein and moist silver oxide (from 10 grams nitrate), as directed; *exactly* precipitate silver with sodium carbonate, filter, and note action of bromine water and alkaline permanganate on portion; distil remainder with dilute sulphuric acid, and repeat tests on acid distillate.]

133. *Olein*.—Note action of olive oil on bromine and permanganate.

[133. *Oleic Acid*.—Freeze stearin from olive oil, and saponify 10 cc. liquid olein with 10 grams litharge and 200 cc. water (reflux). When oil has disappeared, wash and dry soap (test liquid for glycerol), powder and extract with ether; filter, and separate oleic acid as directed. Note action of bromine water and alkaline permanganate.]

## CHAPTER XXV

[136. *Lactic Acid*.—Dissolve 100 grams loaf sugar and 0.5 gram tartaric acid in 500 cc. water. Also leave 150 cc. skim milk to turn sour, and 4 grams of moistened cheese to putrefy, in a warm place. After a week add these, and 50 grams powdered zinc carbonate. Not above 30° or 35°.]

137. *Aldehyde from Lactic Acid*.—Mix 3 cc. of commercial lactic acid with 5 cc. concentrated sulphuric acid; warm *gently* and note carbon monoxide (blue flame). Pour product into 5 cc. water, and distil 1 cc. into some water (use test-tube apparatus, § 19); distillate contains aldehyde—apply silver, rosaniline and resin tests.

137. *Qualitative Tests for Lactic Acid*.—Aldehyde as above. Add a drop of ferric chloride solution to one of phenol, and then some lactic acid; the almost opaque violet changes to bright yellow.

140. *Solid Formulae*.—Cut out a cardboard equilateral triangle, with 2-inch sides. Bisect the sides, and join up the points of bisection. Score with a penknife along the sides of the inner equilateral triangle thus formed, fold it up to a tetrahedron, and fasten with sealing wax. Indicate groups by flag labels fastened to the apices with pins. Try superposition and mirror relations.

## CHAPTER XXVI

[143. *Ethyl Acetoacetate*.—Dissolve 8 grams bright sodium in 80 cc. dry ethyl acetate; proceed as directed; 25 cc. glacial acid, 25 cc. water. Yield 35 per cent. on acetate not recovered. To stop bumping in distillation under reduced pressure, bubbles of air are passed slowly through the

liquid from a fine jet just touching the bottom of the flask; the air is regulated by a clamp at the top (above thermometer, Fig. 20).]

[145. *Acetoacetic Synthesis of Butyric Acid*.—Dissolve 2 grams clean, bright sodium in 25 cc. dry alcohol in a small reflux apparatus; add 10 cc. ethyl acetoacetate, shake, and then add 6 cc. ethyl iodide. Boil on water-bath until neutral (about 2 hours). Distil off alcohol on water-bath, wash residual oil with brine, and separate. Boil the alkylated ester in a reflux apparatus with 10 grams potash in 30 cc. spirit and 5 cc. water; when the action is complete add more water, and boil off the alcohol; then add excess of dilute sulphuric acid, and distil with steam. The butyric acid comes over much faster than the acetic acid; note the odour. Neutralise the early part of the distillate, and isolate calcium butyrate (§ 45); test.]

#### CHAPTER XXVII

[148. *Ethyl Malonate*.—Neutralise 30 grams chloroacetic or bromoacetic acid in 60 cc. water with powdered sodium carbonate; add 19 grams powdered 98 per cent. cyanide, and evaporate on a sand bath until viscid, and temperature of mass is 130°. Break up solid when cold, add 50 cc. spirit, and then, cautiously, a mixture of 12 cc. dry alcohol and 50 cc. concentrated sulphuric acid (in draught). Heat the product on a water-bath; cool; add 60 cc. water, and extract twice with 25 cc. ether. Dry ethereal solution with anhydrous sodium sulphate, distil ether (§ 249), and fractionate. Note b.p. and yield (45 per cent.).]

[148a. *Malonic Acid Synthesis of Butyric Acid*.—On 10 cc. of ethyl malonate. Calculated quantities. Note b.p. and m.p. of ethyl derivatives, and identify butyric acid (yield: 50 per cent. on ethyl malonate).]

149. *Succinic Acid*.—*Qualitative Tests*: Calcium salt soluble, except in presence of alcohol and ammonia. Ferric salt red and gelatinous; no crystals with hydrochloric acid. Acid melts on platinum foil, gives off suffocating fumes, and burns with clear flame. [*Synthesis*: Add 17 grams pure powdered cyanide to 10 cc. ethylene bromide in 80 cc. spirit and 20 cc. water, proceeding as directed. After filtering potassium bromide from cold product, boil with 10 grams caustic soda, and isolate succinic acid. Yield 50 per cent.]

#### CHAPTER XXVIII

154. *Maleic Anhydride*.—Heat 1 gram of commercial malic acid in a test-tube until part of it has sublimed. Scrape out sublimate of maleic anhydride, boil with water, and cool. Note acidity of resulting solution, decolorisation of bromine water, and (after neutralisation) of cold, dilute, alkaline permanganate.

#### CHAPTER XXIX

159. *Tartaric Acid*.—Prepare from 30 grams argol. Note m.p.; test.

159. *Qualitative Tests for Tartaric Acid*.—Chars on heating; burnt sugar odour. Calcium salt (calcium chloride and neutral tartrate) appears in cold, but is soluble in acetic acid and caustic soda; reappears on boiling



latter solution. Tartrate to copper sulphate prevents precipitation of oxide by caustic soda, simply dark blue solution. Tartrates reduce ammoniacal silver nitrate (distinction from citrates). Potassium hydrogen tartrate (potassium chloride and acetic acid) is sparingly soluble, and appears on rubbing sides of tube. A drop of ferrous sulphate solution, followed by a drop of hydrogen peroxide, and then caustic soda, drop by drop, gives a violet colour.

[159. *Ethyl Tartrate*.—Dissolve 15 grams powdered tartaric acid in 45 cc. dry alcohol (on water-bath), add 15 cc. dry alcohol, previously saturated cold with dry hydrogen chloride, and boil on water-bath for 3 hours. Cool, expel bulk of hydrogen chloride by aspirating dry air, and distil off excess of alcohol well below 70°, in a good vacuum; carefully neutralise remaining acid with dilute ammonia, and leave syrupy residue in a basin in a vacuum desiccator over quicklime. Next day pour off from ammonium chloride, and distil under diminished pressure (165° at 20 mm.). Note solubility of a drop of the ester in water. Yield 70 per cent. Add excess of acetyl chloride, warm to complete the action, cool and add an equal volume of water; the *ethyl acetyltartrate* separates as an oil, which eventually crystallises. Recrystallise from water, and take m.p., 60°.]

[160. *Dihydroxymaleic Acid*.—Dissolve 10 grams tartaric acid in 5 to 10 cc. of hot water, add 0.1 gram of reduced iron and keep hot until dissolved. Cool in ice, and add 20 volume hydrogen peroxide (*keeping ice-cold*) until colour has changed through yellow and dark green to black (mix well). Draw out a thistle-funnel to a narrow jet, and add through it in small quantities (*keeping ice-cold*) one tenth the total volume of Nordhausen sulphuric acid. Keep in ice overnight, drain crystals at pump, and wash with ice-water. Yield 40 per cent. Powerful acid; gives with ferric chloride a blackish colour, which is turned intense violet by alkalies (destroyed by excess). Warm with water to 60°; brisk effervescence of carbon dioxide; glycollic aldehyde remains, which test (§ 121).]

[161. *Racemic Acid*.—Heat 5 grams of Rochelle salt with 10 grams caustic soda in 15 cc. water (small reflux, sand-bath, 1 hour, nearly boiling); dilute, and *nearly* neutralise with hydrochloric acid; acidify with acetic acid, and add a strong solution of calcium chloride, stirring well. Collect and wash precipitated calcium racemate, and apply tartaric tests.]

163. *Solid Formulae of Tartaric Acids*.—Fasten pairs of tetrahedra together with wire fasteners before sealing up. Six tetrahedra are wanted for a complete set.

164. *Qualitative Tests for Citric Acid*.—Calcium salt appears only on boiling. Citrates do not reduce silver. Acid potassium salt is soluble.

164. *Conversion of Citric Acid into Acetone*.—Cover 10 grams of citric acid crystals with concentrated sulphuric acid, in a small flask furnished with cork and gas jet. Warm gently, until the evolved gas ceases to burn with a blue flame (carbon monoxide). Continue heating until the product shows signs of charring (prove carbon dioxide is evolved). Cool, mix with an equal bulk of water, and distil with thermometer in vapour until 90° is reached. Prove distillate is dilute acetone: phenylhydrazine, bisulphite, and oxidation with hypochlorite and permanganate (§§ 88-90).

## CHAPTER XXX

167. *Qualitative Tests for Cane Sugar.*—Non-volatile. Syrup or crystals when evaporated on water-bath. Chars with heat or concentrated sulphuric acid; burnt sugar odour. Pale yellow with boiling caustic soda. No reduction of alkaline copper tartrate, unless solution is previously boiled with a drop of dilute hydrochloric acid and neutralised. No osazone.

[167. *Estimation of Cane Sugar.*—Invert 100 cc. of solution, which should contain about  $\frac{1}{10}$ th of its weight of sugar, by heating it at 100° for 15 minutes with 0.5 cc. concentrated hydrochloric acid. Neutralise with sodium carbonate, make up to 500 cc., and then as with glucose (below); 10 cc. Fehling's solution = 0.0475 gram cane sugar.]

\* 168. *Hydrolysis of Cane Sugar.*—Heat solution of  $\frac{1}{2}$  gram sugar in 50 cc. water with a few drops of dilute hydrochloric acid on a water-bath for 15 minutes. Neutralise with sodium carbonate, and test with alkaline copper tartrate, as with glucose. Test original sugar solution also.

168. *Glucose.*—Add 35 grams powdered cane sugar by degrees (as dissolved) to 100 cc. spirit with 4 cc. concentrated hydrochloric acid, keeping at 45°. In a few days at the ordinary temperature the glucose (being less soluble than the accompanying fructose) crystallises out. Drain at the pump, or on a plate, and recrystallise from dilute methyl alcohol: add the hot alcohol to the hot syrup until slightly turbid, clear with a drop or so of hot water, and allow to cool. Yield 50 per cent.

168.—*Qualitative Tests for Glucose.*—Melting point. Non-volatile. Sweet syrup when evaporated on water-bath. Not blackened by concentrated sulphuric acid, if pure. Dark brown product with boiling caustic soda. Reduces alkaline copper tartrate on warming (2 grams copper sulphate and 10 grams Rochelle salt in 20 cc. water; keep this, and add to 1 cc. just before use the same volume of a solution of 3 grams caustic soda in 20 cc. water). Reduces ammonio-silver nitrate. Reduces copper-acetic solution on boiling for 2 minutes (see § 170). Reduces bismuth hydroxide (bismuth nitrate and caustic soda). Crystalline osazone (§ 185).

[168. *Estimation of Glucose.*—Fehling's solution: Copper and alkaline tartrate solutions mixed just before use, as mixed solution does not keep well. Solution A: 17.32 grams recrystallised copper sulphate (exactly weighed) dissolved in 150 cc. water, and cold solution made up to exactly 250 cc. Solution B: 35 grams caustic soda and 90 grams recrystallised Rochelle salt dissolved in 150 cc. water, and cold solution made up to exactly 250 cc. To estimate sugar in solution, place 5.00 cc. A, and 5 cc. B in small flask, with 40 cc. water (and piece of porous plate to check bumping), and boil. Then run in sugar solution from burette, cautiously, until colour of supernatant liquid is just faintly yellow after precipitate has settled (white paper behind flask). 1 mol. glucose (180) reduces 5 mols. copper sulphate (1247), so that 5 cc. of latter (0.3464 gram) = 0.05 gram glucose; this is therefore the quantity in the amount of solution required to decolorise the copper. If the strength of the sugar solution is less than  $\frac{1}{2}$  gram or more than 1 gram per 100 cc., the results are only approximate, and the estimation must be repeated on a more concentrated or dilute solution. If Fehling's solution is old, check by inverting 0.475 gram cane sugar (§ 167), and making up to 100 cc.; 10 cc. of this should just decolorise 5 cc. of copper sulphate.

170. *Milk Sugar*.—Curdle 100 cc. milk at 30° with one drop of hydrochloric acid. Evaporate filtered and neutralised whey to syrup; cover up and leave to crystallise. *Qualitative Tests*.—Gritty and only slightly sweet. Sparingly and slowly soluble in cold water. Does not blacken when heated with concentrated sulphuric acid. Does not colour with caustic soda. Reduces alkaline copper tartrate, but does not reduce copper-acetic solution on boiling for 2 minutes (1 gram copper acetate, 25 cc. water, 20 drops B.P. or 8 drops glacial acetic acid). Forms osazone, characteristic crystals.

[170. *Estimation of Milk Sugar*.—As with glucose, but 5 cc. copper sulphate = 0.067 gram lactose.]

172. *Fermentation of Glucose*.—Add a teaspoonful of yeast to 5 grams glucose in 100 cc. water, in a large flask with delivery tube; and keep at 30°. Note carbon dioxide, and when action is finished, distil and test for alcohol.

173. *Hydrolytic Action of Diastase*.—Shake 5 grams starch (commercial starch, washed with cold water, and dried on porous plate) with 100 cc. water, and heat on water-bath, with constant shaking, until the whole has become a homogeneous, translucent jelly. Test with iodine (cold), phenylhydrazine, and Fehling (§ 173). Now cool to 30°, add 5 cc. malt extract, and shake well; the stiff jelly rapidly becomes liquid. Test again as above; the starch has been converted into maltose.

## CHAPTER XXXI

176. *Starch*.—Separate starch from flour as indicated. Allow to settle; drain; dry on porous plate. *Qualitative Tests*.—Insoluble in cold, soluble in hot water. Blue iodide with iodine in potassium iodide; decolorised by heat, colour returns on cooling. No copper reduction. No hydrazone. Hydrolysis to glucose, which reduces copper, and gives hydrazone.

[177. *Estimation of Starch*.—Heat 1 gram with 100 cc. water and 10 drops concentrated sulphuric acid, in an open flask on a water-bath (30–60 minutes), until a drop of the solution (cooled) ceases to give blue with iodine. Then neutralise with soda and proceed as with glucose; 5 cc. copper sulphate = 0.0455 gram starch.]

177. *Hydrolysis of Starch*.—Rub 2 grams to cream with 10 cc. water, make up to 200 cc., and heat on water-bath until a homogeneous jelly. Boil portion of this with a few drops of dilute sulphuric acid for a few minutes, and neutralise; test with copper, caustic soda and phenylhydrazine (§ 185). *Dextrin*.—Moisten 5 grams starch with 5 drops of dilute sulphuric acid, and heat in test-tube in sulphuric acid bath at 200° for an hour. The brownish product is now soluble in cold water; it reduces copper, and gives either a red colour or no colour with iodine, but no precipitate with phenylhydrazine acetate.

178. *Cellulose*.—Add excess of concentrated ammonia to washed copper oxide, previously precipitated by caustic soda from a boiling solution of 2 grams copper sulphate in 50 cc. water; the oxide dissolves to a deep-blue solution (Schweizer's solution). Add filter paper to this as long as it disappears; the paper gelatinises and slowly dissolves; ordinary unsized paper thus treated superficially and then dried, is rendered water-proof

(roofing paper, etc.) Filter and add excess of dilute sulphuric acid; collect, wash and dry gelatinous precipitate of cellulose.

178. *Hydrolysis of Cellulose*.—Dip strips of thick filter paper for a few seconds in a cold mixture of 10 cc. concentrated sulphuric acid and 5 cc. water; transfer to water and wash until free from acid; hang on glass rod until dry: the paper is converted into tough, translucent, vegetable parchment. Immerse strips of filter paper in 5 cc. warm (not hot) concentrated sulphuric acid; they swell up and dissolve; dilute with 30 cc. water, boil vigorously, neutralise with calcium carbonate (whitening, as §25); filter, and test for glucose. Dip strips of white calico in a cold solution of 5 grams caustic soda in 5 cc. water; when the fabric has shrunk considerably, wash with water, remove residual alkali with dilute hydrochloric acid, and finally wash with water and dry on glass rod. The shrunken fibres have become smooth and glossy ("mercerised").

[178. *Cellulose Nitrate*.—As directed. Do not convert more than 0.5 gram of cotton, and destroy product after testing.]

## CHAPTER XXXII

[180. *Acetylation of Glucose*.—Boil 3 grams of glucose crystals with 10 cc. of acetic anhydride and a very small fragment of zinc chloride for 15 minutes (sand-bath, with plain reflux tube); evaporate twice to dryness on a water-bath, first alone, and then with alcohol; extract pentacetyl-glucose with hot, absolute alcohol, and crystallise. Determine melting-point, 112°. Yield 50 per cent. Boil some pentacetyl-glucose with 50 per cent. sulphuric acid, dilute and distil; test distillate for acetic acid, and residue (after neutralising) for glucose. See also Benzoylation, § 270.]

[180. *Mannitol and Sorbitol*.—Invert 10 grams cane sugar (§ 168). Reduce with sodium amalgam in acid solution (as with aldehyde, § 83), and note that the copper reducing power eventually vanishes. Evaporate to dryness on a water-bath (separating sodium sulphate), and extract with strong spirit; make benzoyl derivative (§ 270).]

[180. *Hexyl Iodide*.—Add yellow phosphorus in small pieces (about 6 grams) cautiously to 20 grams iodine and 20 cc. water in a distilling-flask, until the iodine has disappeared. Then add 10 grams of commercial mannitol, and after the energetic action is over, distil from an oil-bath in a current of washed carbon dioxide. Add small pieces of yellow phosphorus to the distillate until it is colourless, pour back, and redistil, repeating this operation until the hexyl iodide comes over free from iodine. Dry, and take boiling-point. Yield 70 per cent. Reduce some hexyl iodide to hexane with zinc and dilute hydrochloric acid, in a small reflux apparatus. Wash, dry, note boiling-point, and prove there is no action with bromine water, or alkaline permanganate.]

[181. *Gluconic Acid and Lactone*.—Add yellow mercuric oxide to a boiling solution of 5 grams of glucose in 50 cc. water, until it ceases to be reduced (test filtered portion by boiling with more oxide). Precipitate the mercury from the resulting mercurous gluconate by hydrogen sulphide, and evaporate filtrate to dryness. Gluconic lactone is left (yield 50 per cent.); no reaction with Fehling if free from glucose. Reduce the aqueous lactone solution cautiously with sodium amalgam, keeping slightly acid

with dilute sulphuric acid, pour off from mercury from time to time, and test for glucose with Fehling. (See Mannitol, below.)]

[181. *Saccharic Acid*.—Cane sugar 20 grams, nitric acid 30 cc., water 15 cc.; proceed as directed.]

### CHAPTER XXXIII

185. *Glucosazone*.—Mix 2 grams glucose in 15 cc. water with solution of 2 grams phenylhydrazine in just sufficient dilute acetic acid; both filtered. Heat in small flask in beaker of boiling water; wash; dry. Recrystallise from alcohol. Take m.p. by capillary tube method.

186. *Mannose*.—Add solution of 1 gram ferrous sulphate (made in cold) to solution of 4 grams mannitol in 20 cc. water; then add gradually 12 cc. of 20 volume hydrogen peroxide (or proportionally more of weaker peroxide), *keeping cool*. Make the product just alkaline with sodium carbonate, filter, and test a small portion for mannose, as for glucose. To bulk add cold solution of 1 cc. phenylhydrazine in a slight excess of dilute acetic acid; after an hour, filter and wash precipitate of mannose phenylhydrazone, and dry on porous plate. Yield 30 per cent. Recrystallise from dilute alcohol (§ 168) until colourless, and take melting-point, 198°.

187. *Synthesis of Hexoses*.—Dilute 20 cc. 40 per cent. formaldehyde with 180 cc. water, and add finely powdered slaked lime until saturated. Filter, and keep in corked flask for a week. *Exactly* precipitate lime with dilute oxalic acid, concentrate filtrate on water-bath, and apply glucose tests. Osazone is a mixture, with indefinite melting-point.

### CHAPTER XXXIV

191. *Urea from Urine*.—Evaporate 100 cc. fresh urine to one-sixth, on a water-bath. Cool syrup and add cautiously 16 cc. concentrated nitric acid, *keeping cool*; pour off *mother liquor* from nitrate, and drain on porous plate. Redissolve in a few cc. of cold water, reprecipitate with concentrated nitric acid, and drain on plate again. Barium carbonate as cream with water. Take melting-point. Apply tests. *Qualitative Tests*.—Non-volatile. Crystalline residue on evaporation, especially from alcohol. Nitrate. Ammonia with concentrated soda only. Hypobromite. Cyanurate. Urea nitrate only gives the brown ring test, when the solution is mixed with twice its volume of concentrated sulphuric acid, and the ferrous sulphate floated on it, cold.

191. *Hydrolysis of Urea*.—Boil 1 gram with very strong caustic soda solution—2 grams in 2 cc.; prove ammonia and carbonate. Nitrous acid as with acetamide—1 gram; prove nitrogen and carbon dioxide—one-third soluble in caustic soda. Hypobromite: Fill test tube with caustic soda, to which bromine has been added (keeping cool) until deep yellow; invert in small basin of soda; introduce quickly  $\frac{1}{2}$  gram dry urea crystals (packed tightly in short tube closed at one end), and compare volume of nitrogen with theoretical.

[191. *Estimation of Urea*.—Dissolve 2 cc. of bromine, *without rise of temperature*, in 20 cc. of 40 per cent. caustic soda, in a 200 cc. flask (the colour should be yellow), and pass a small test tube, with 5 cc. of the urine, down the neck, without spilling. Cork the flask, place in a beaker of cold water, and connect through cork, by glass and rubber tube, with a clip burette, which is nearly filled with water and inverted in cylinder of water. The burette is now raised or lowered until the level of the water is the same inside and outside, and the reading is noted. The clip is next opened, and the urine slowly poured into the hypobromite by tilting the flask, the clip being left open until the latter has regained its original temperature. Finally, the burette is raised until the water is again level, and the reading taken. Difference between two readings = no. of cc. of nitrogen;  $37.1$  cc. of moist nitrogen at  $18^{\circ}$  and  $760$  mm. =  $0.1$  gram urea, or no. of cc.  $\times 2.7$  = no. of milligrams of urea in sample. In Allen's modification  $2\frac{1}{2}$  times weight of potassium cyanate is added to urea, to prevent, by mass action, reconversion of urea into ammonium cyanate, and the bromine, in aqueous potassium bromide, is added to the mixture of the urea-cyanate solution with the soda.]

[192. *Synthesis of Urea from Cyanide*.—Thoroughly fuse 10 grams powdered 98 per cent. potassium cyanide with 15 grams red lead, in iron spoon or dish. Powder, and boil with 30 cc. water; filter; add 10 grams ammonium sulphate, and evaporate dry on a water-bath. Powder again, and extract with hot spirit in reflux apparatus; crystallise. Yield 30 per cent. Take melting-point. Apply tests. *Alternative method*.—Add gradually a cold solution of  $6\frac{1}{2}$  grams permanganate in 100 cc. water to a cold solution of 4 grams 98 per cent. cyanide and 10 grams caustic potash in 25 cc. water, *keeping temperature below  $20^{\circ}$* . Next day add a solution of 7 grams ammonium sulphate in 20 cc. hot water, boil, filter, and wash precipitated manganese dioxide with a little boiling water. Evaporate to dryness on water-bath, and extract with hot spirit as before. Yield 60 per cent.

[193. *Condensation of Urea*.—Heat  $\frac{1}{2}$  gram at  $200^{\circ}$  in dry test tube in sulphuric acid bath; note ammonia; dissolve in dilute caustic soda, and add two or three drops of *very dilute* copper sulphate—violet biuret colour. Dissolve 1 gram urea in dilute hydrochloric acid and evaporate to dryness on a water-bath; heat as directed, and convert half the residue into the barium salt—very little ammonia and barium chloride. Heat the other half strongly in a dry test tube, and note the pungent odour of cyanic acid.

## CHAPTER XXXV

[195. *Uric Acid*.—Saturate 100 cc. of urine with ammonium chloride (about 30 grams are required), add ammonia (a few drops), and after 15 minutes filter. Pierce filter, wash precipitate into test tube with a little water, dissolve in very little boiling caustic soda, cool, and filter. Acidify filtrate with dilute hydrochloric acid. Uric acid is slowly precipitated; collect, wash, and apply murexide test. *Qualitative Tests*.—Insoluble in water and dilute acids; soluble in alkalis. Murexide test.

[195. *Estimation of Uric Acid in Urine*.—(Precipitate as ammonium urate and titrate with dilute permanganate). Saturate 100 cc. urine with

finely powdered ammonium chloride as above, stirring vigorously; add a few drops of ammonia, still stirring, and after 15 minutes transfer to a filter, and wash with a saturated solution of ammonium sulphate, until no chloride remains. Rinse precipitate of acid ammonium urate from filter with hot water, dilute to 100 cc. with cold water, and add 20 cc. concentrated sulphuric acid, and stir, thus raising temperature to about 60°. Then quickly run in permanganate ( $N/20 = 1.578$  grams per litre) until pink tint ceases to vanish *instantly* on shaking; further decolorisation may occur on standing, but this is to be disregarded. 1 cc. permanganate = 0.00375 gram uric acid.]

[196. *Alloxan*.—Add 5 grams of uric acid (precipitated from concentrated sulphuric acid, washed and dried), to 10 cc. concentrated nitric acid diluted with 5 cc. water (=sp. gr. 1.3). Proceed as directed.]

[196. *Urea (and Allantoin) from Uric Acid*.—On 5 grams as directed. Test urea.]

[198. *Caffeine from Tea*.—Boil 28 grams (1 ounce) of China tea with 200 cc. water for 10 minutes, strain hot through calico, squeeze dry and wash in same way with 100 cc. water; mix, cool, and add basic lead acetate (lead acetate boiled with excess of litharge and filtered), as long as a precipitate is formed. Filter, precipitate most of the lead with dilute sulphuric acid, and the remainder with sulphuretted hydrogen (to avoid free sulphuric acid). Evaporate on water-bath to 10 cc. and shake twice in a tap-funnel with 10 cc. of chloroform. Separate, and distil off chloroform on water-bath. Dissolve residue in a few drops of water, adding a drop of dilute hydrochloric acid, and evaporate on a watch-glass. Yield not more than  $\frac{1}{2}$  gram. Apply murexide test.]

## CHAPTER XXXVI

[201. *Synthesis of Potassium Cyanide*.—Distil 10 grams of synthetic ammonium thiocyanate (§ 210) gently (*in draught*) with dilute nitric acid (concentrated acid with twice its volume of water); when the thermometer in the distilling vapour reaches 80°, mix the distillate with 5 volumes of strong spirit, and add a solution of 3 grams of caustic potash in 3 cc. water. If there is no precipitate of potassium cyanide, add a little ether. Collect the precipitate, and drain on porous plate. Test as below.]

[201. *Potassium-Sodium Cyanide from Ferrocyanide*.—Heat 10 grams potassium ferrocyanide in a water-bath (flask), in a stream of dry air (sulphuric acid), until it falls to a white powder, transfer the powder to a Rose's crucible, and fuse with 1 gram of clean sodium in a gentle stream of coal-gas. Pour clear melt on clean iron slab or broken porcelain. Test as below.]

201. *Qualitative Tests for Cyanides*.—Prussian blue test: add ferrous sulphate, ferric chloride and caustic soda; warm, then add excess of hydrochloric acid. Thiocyanate test: evaporate hydrocyanic acid to dryness with yellow ammonium sulphide on water-bath; ferric chloride gives red ferric thiocyanate. Silver test: silver cyanide, like silver chloride, is insoluble in dilute nitric acid, soluble in ammonia; it is also soluble in excess of cyanide. These three tests are best made in watch-glasses, inverted over small beakers, containing the cyanide, with some warm dilute hydrochloric

acid, the glass being smeared with caustic soda, ammonium sulphide or silver nitrate, and left 15 minutes. (Mercuric cyanide is not ionised, and must first be decomposed by metallic zinc.)

[201. *Estimation of Hydrocyanic Acid.*—The cyanide is dissolved in, or diluted with, water, rendered faintly alkaline by adding caustic soda (to the acid, or dilute nitric acid to the alkaline solution), and kept in this state throughout the operation (colour with litmus). Silver solution (4.25 grams per 250 cc.  $\text{AgNO}_3$ /10 per litre) is run in quickly until there is a slight, but permanent turbidity of silver cyanide. The alkali cyanide is converted into the double cyanide; 1 cc. silver = 0.0054 gram hydrogen cyanide ( $=2\text{HCN}/10$ ).]

202. *Potassium Ferrocyanide and Ferricyanide.*—Boil a solution of 5 grams potassium cyanide and 1 gram of caustic potash in 25 cc. of water, with one of 3 grams crystallised ferrous sulphate in 25 cc. water (if the precipitate is blue add more alkali); filter, concentrate, and crystallise; test ferrocyanide. Add bromine to hot solution of 3 grams of ferrocyanide until ferric chloride ceases to give a blue precipitate with a drop; crystallise, and test ferricyanide. Heat 2 grams powdered ferrocyanide to redness in a hard-glass test tube; break up, powder, and boil with water; evaporate filtered solution, and test for simple cyanides.

203. *Qualitative Tests for Ferrocyanides and Ferricyanides.*—Ferrocyanides: ferric salts dark blue; ferrous salts light blue; copper salt, chocolate; carbon monoxide with warm concentrated sulphuric acid, hydrocyanic acid with dilute sulphuric acid; insoluble ferrocyanides are decomposed by caustic soda. Ferricyanides: brown colour with ferric, dark blue precipitate with ferrous salts.

[203. *Ethyl Isocyanide.*—Boil 2 cc. of ethyl iodide gently on water-bath (in small flask with long reflux tube) with 6 grams dry silver cyanide (precipitate 10 grams nitrate with excess of dilute, distilled hydrocyanic acid), until liquid ceases to run back, and mass is pasty (about 1 hour). Now add solution of 2 grams powdered 98 per cent. potassium cyanide in 5 cc. water, and distil from a water-bath (same flask). Insoluble distillate, nauseously bitter. Divide in two portions. To one add remainder of silver cyanide, cautiously; it dissolves with energy to a soluble, crystalline double cyanide. To the other, add concentrated hydrochloric acid drop by drop; there is a violent action, and the unpleasant odour disappears; dilute, add excess of caustic soda, and distil ethylamine into a little water; test.]

## CHAPTER XXXVII

207. *Ethyl Isocyanate.*—Distil some ethyl sodium sulphate with potassium cyanate (§ 192) from a dry test tube. Note pungent, unpleasant odour of isocyanate or carbimide. Boil with potash, and note ethylamine.

[209. *Mercuric Fulminate.*—Dissolve 1 gram of mercury in 10 cc. nitric acid, and add cautiously, in small portions, to 15 cc. of 90 per cent. spirit. When the action is over, allow to cool; crystals of mercuric fulminate separate. Place a single small crystal on filter paper, and when dry, hammer smartly; it detonates violently. Wash the remaining crystals with spirit



by decantation, and add excess of concentrated hydrochloric acid; when they are dissolved (*but not before*), dilute somewhat, and boil vigorously to destroy the mercuric formate. Filter off the mercurous chloride, make alkaline with caustic soda, and add Fehling's solution; it is reduced by the hydroxylamine.]

210. *Ammonium Thiocyanate*.—Mix 20 cc. concentrated ammonia, 20 cc. spirit, 3 cc. carbon bisulphide. Proceed as directed. Evaporate residue to dryness on a water-bath, extract with hot spirit, crystallise and test. *Qualitative Tests*.—Ferric salt is blood-red, unaffected by dilute nitric acid, but decolorised by mercuric chloride; silver salt insoluble in nitric acid.

210. *Mustard Oil* (see also Aniline).—From methylamine or ethylamine and carbon bisulphide (1 drop), warmed with ferric chloride, and sufficient alcohol to make the solution homogeneous; note pungent odour.

#### CHAPTER XXXVIII

212. *Methylamine*.—Mix 5 grams acetamide with 4½ cc. bromine, and add a solution of 5 grams caustic soda in 50 cc. water until product is yellow. Run this product, through a thistle funnel, into a distilling flask, containing 12 grams caustic soda in 36 cc. water at 70°—*not above* (condenser to dip under little water in receiver). Then proceed as in § 57 for methylamine hydrochloride crystals.

212. *Methylamine Hydrochloride*.—Dissolve 25 grams ammonium chloride in 50 cc. 40 per cent. formaldehyde, and distil from a water bath, gradually raising the temperature from 40° to 100° (thermometer *in solution*); volatile *methylal* distils (redistil, and note b.p.). When distillation ceases, transfer the chloride solution to a dish, and evaporate on a water bath to incipient crystallisation; cool, filter off ammonium chloride (*at pump*), and continue evaporation until whole product solidifies on cooling. Recrystallise from spirit. Yield 70–80 per cent.

Heat 2 grams with equal bulk of soda-lime in test-tube with jet: examine alkaline organic vapour, as in § 57. Distil 2 grams with caustic soda, and collect in 5 cc. water; compare solution with ethylamine solution, § 57. Dissolve 1 gram in spirit, and add 5 drops of chloroform and some caustic soda crystals, warming if necessary; note unpleasant odour of isocyanide.

#### CHAPTER XXXIX

217. *Glycine*.—Dissolve 18 grams ammonium chloride in 50 cc. 40 per cent. formaldehyde, in a 200 cc. flask kept cool in ice-water; and add at intervals, over 3 hours, with much shaking (larger quantities require a mechanical stirrer) a cold solution of 22 grams 98 per cent. potassium cyanide in 30 cc. water; during the last 1½ hours add, also slowly, 13 cc. glacial acetic acid. Separate the crystalline product (methylene-amino-acetonitrile) at the pump (or collect on filter), and drain on porous plate.

Yield 60 per cent. Cover product with 20 cc. cold alcohol, previously saturated with hydrochloric acid; after an hour dilute with 100 cc. water, distil off alcohol, and evaporate residual liquid to dryness on a water-bath. Recrystallise glycine from dilute alcohol. Yield 80 per cent. calculated on methylene compound. Take m.p. Note sweet taste, neutral.

Methylamine with soda-lime (odour, reaction and inflammability). Nitrogen with nitrous acid, as with ethylamine. Dissolve some freshly precipitated copper oxide in solution of  $\frac{1}{2}$  gram, and evaporate filtered solution for copper amino-acetate.

219. *Diazo-Ester test*.—As directed.

222. *Albumen*.—Test filtered solution of egg-white. Coagulated by heat and nitric acid. Yellow with excess of concentrated nitric acid (xanthoproteic test). Violet with drop of very dilute copper sulphate, followed by caustic alkali (biuret test). Red precipitate with solution of 1 drop of mercury in excess of concentrated nitric acid (Millon's test). Purple ring with drop of glyoxylic acid (§ 121), and concentrated sulphuric acid (Hopkins' test).

224. *Amino-Acids from Gelatine*.—Boil 1 gram gelatine in reflux apparatus with 10 cc. alcoholic hydrochloric acid for an hour (water-bath); evaporate to dryness, and apply diazo-ester test (§ 219).

## CHAPTER XLI

[230. *Ethyl Nitrate*.—Add 1 gram urea to 4 cc. acid, and run cautiously into mixture 10 cc. dry alcohol; distil from water-bath. *This preparation is dangerous*, as ethyl nitrate is liable to explode when heated.]

230. *Ethyl Nitrite*.—Warm a little alcohol with copper turnings and a few drops of concentrated nitric acid in a test tube, and note odour.

230. *Amyl Nitrite*.—Mix 15 grams *dry*, powdered sodium nitrite with 17 cc. ice-cold amyl alcohol, and add slowly, with much shaking, 5 cc. ice-cold concentrated sulphuric acid. Dilute by pouring on 20 grams of crushed ice, and separate the floating layer of amyl nitrite; dry with calcium chloride and distil. Yield 70 per cent. Note peculiar, oppressive odour. Hydrolyse a little by shaking with 50 per cent. potash; when the milky emulsion clears and the odour has gone, dilute with water and distil off the alcohol with the steam; test the distillate, and prove nitrite in residue.

[231. *Nitromethane*.—Mix warm solutions of 14 grams silver nitrate in 10 cc. water and 9 grams potassium nitrite in 10 cc. water; cool, collect precipitated silver nitrite on filter, and dry on porous plate (covered, and away from light). Place 11 grams silver nitrite, mixed with an equal bulk of dry sand, in a small reflux apparatus, add 4½ cc. methyl iodide, and heat on water-bath for 2 hours. Then distil from water-bath. Yield 70 per cent.

Add a few drops of the crude nitromethane to 2 cc. of clear alcoholic sodium methoxide (sodium in dry methyl alcohol), and note crystalline precipitate of sodium isonitromethane; collect this on a small filter, dissolve *at once* in water, and add ferric chloride; note crimson ferric compound. Dissolve the rest of the nitromethane in dilute caustic soda (filter off unchanged iodide); to a small portion add a crystal of potassium nitrite, acidify with dilute sulphuric acid, and then make alkaline with

caustic soda; note crimson nitrolate. Distil the remainder of solution with granulated zinc, and collect distillate in a little water; prove methylamine.]

## CHAPTER XLII

236. *Detection of Phosphorus*.—Heat some hard egg-yolk to redness with magnesium powder, and when cold, add water; note odour of phosphine.

[236. *Estimation of Phosphorus*.—As with sulphur; the phosphoric acid is converted into magnesium pyrophosphate in the usual manner.]

237. *Cacodyl*.—In very small quantity by heating dry sodium acetate (a few milligrams), with an equal amount of white arsenic; note foul odour (the vapour is poisonous, and produces nausea if inhaled).

[239, 240. *Mercaptan and Sulphonol*.—Distil 9 grams ethyl sodium sulphate with hydrosulphide from 3 grams caustic soda in 5 cc. water, as directed (convert a few drops of distillate into mercury compound). Mix the mercaptan with half its volume of acetone; saturate with dry hydrogen chloride, neutralise with soda, and distil the liquid *mercaptol* from a water-bath, under low pressure (§ 143). Oxidise mercaptol with 5 per cent. permanganate ( $7\frac{1}{2}$  grams in 150 cc. water) in reflux apparatus, adding a few drops of dilute sulphuric acid from time to time, as necessary. Filter hot, evaporate, and crystallise resulting sulphonol. Take m.p.]

## PART III

### CHAPTER XLIII

[243. *Benzene from Commercial Product.*—Fractionate 100 cc. "light oil" if procurable, or 100 cc. "50 per cent. benzene" (known commercially as 50 per cent. "benzol"), reserving portion boiling above  $100^{\circ}$  (for § 279); boil lower fraction in a reflux apparatus with 20 cc. spirit and 5 grams caustic potash, to eliminate carbon disulphide (0.2 to 0.3 per cent.); pour into water, separate light layer of benzene, shake repeatedly with concentrated sulphuric acid, and re-fractionate until fraction  $79-81^{\circ}$  is obtained; then freeze until melting-point is constant; take sp.gr. Benzene vapour is *very heavy and inflammable*.

243. *Characteristics of Pure Benzene.*—Freezes in ice (take m.p.). Does not decolorise bromine water (dissolves the bromine) or cold dilute alkaline permanganate (§ 104), when shaken with these, nor blacken with concentrated sulphuric acid. Burns with very smoky flame; contrast with "benzoline" (volatile paraffins).

244. *Bromobenzene.*—Add cautiously, through reflux condenser (tap-funnel through upper cork, Fig. 18), 10 cc. bromine to 17 cc. *crystallisable* benzene, containing  $\frac{1}{4}$  gram iron filings: long tube of Volhard trap just through the cork; the bent tube to *bottom* of each flask; the second cork loose, or with extra hole; 20 cc. water in trap. Keep hydrogen bromide for § 260. Proceed as directed. In steam distillation, an ordinary flask may be substituted for the distilling flask (see Fig. 15); tilt to keep spray from condenser. Wash with dilute soda before drying. Note b.p., sp.gr., and halogen flame. Keep for §§ 267, 279. Yield 50 per cent. Drain dibromobenzene on porous plate, and recrystallise as directed; take m.p. Yield 15 per cent. (variable).

246. *Nitrobenzene.*—Add 20 cc. sulphuric acid to 18 cc. nitric acid; cool, and add slowly, *with much shaking* (use fairly large flask) to 20 cc. *crystallisable* benzene. Pour product into beaker of cold water, and proceed as directed. Note b.p. and sp.gr. Yield 80 per cent.

247. *Sodium Benzene-Sulphonate.*—Digest 40 cc. benzene with 80 cc. concentrated or fuming acid as directed. Sodium salt as in § 25. Brine method; pour into 4 volumes saturated, ice-cold brine, cool to  $0^{\circ}$ , and stir (if there are no crystals in 10 minutes, cool 10 cc. in ice and salt, and add crystals so obtained); after half an hour drain at pump, and recrystallise from alcohol. Test for sulphur. Yield 70 per cent.

247. *Benzene-Sulphonic Chloride.*—Mix 10 grams sulphonate, 15 grams pentachloride; as directed; 10 cc. ice-water. Distil ether from water-bath (§ 249), and chloride from test-tube over gauze. Note b.p. and odour. Prove sulphur and chlorine (hydrolyse). Yield 60 per cent.

247. *Benzene-Sulphonamide*.—Use remainder of chloride; 10 grams carbonate per cc.; heat on water-bath until odour is gone. Recrystallise from spirit (§ 244); take m.p. Prove sulphur and nitrogen. Hydrolyse with caustic soda (test-tube), and prove ammonia. Yield 80 per cent.

## CHAPTER XLIV

249. *Aniline*.—Use 20 cc. nitrobenzene and 45 grams tin, adding 90 cc. concentrated hydrochloric acid in 10 cc. portions, and waiting each time for action to subside (warm to start); heat until odour of nitrobenzene has disappeared; cool and add 85 grams of caustic soda powder in 100 cc. water (keeping cool), until product is grayish and fairly limpid. Steam distil from large flask. Collect drops of aniline, dry with solid caustic soda, and pour off. Dissolve 5 grams caustic soda in the water, shake with 10th volume of ether, and separate. Repeat extraction. Dry mixed extracts with stick of soda, pour off, and distil ether from water bath (no flame; the ether may be used for other extractions); then whole of aniline over gauze (Fig. 22). Note b.p. Test. Yield 80 per cent.

249. *Qualitative Tests for Aniline*.—Odour (alkali if necessary). Pure liquid precipitated by hydrochloric acid. Isocyanide. Mustard oil. Nitrogen and phenol with nitrite. Violet with bleaching solution; brick-red with hypobromite; yellowish precipitate with bromine water. Blue with a few drops of bichromate added to solution in concentrated sulphuric acid. Smear a little on a wooden match, and moisten with hydrochloric acid: the wood is stained bright yellow.

250. *Methylaniline*.—Dissolve 2 cc. commercial methylaniline in dilute hydrochloric acid and add a solution of 1 gram sodium nitrite in 2 cc. water; note precipitated oil. Extract with a few cc. ether, and allow to evaporate on watch-glass; note odour of *nitrosamine*. Add a drop to some phenol-sulphonic acid (crystal of phenol in 5 cc. concentrated acid) and warm: blue (Liebermann's nitroso-reaction, § 254).

251. *Acetanilide*.—Boil 10 cc. aniline with 10 cc. glacial acid for at least four hours. Distil as with acetamide; anilide passes over above 280°. Recrystallise from hot water (filter hot); take m.p. Yield 80 per cent. Repeat with 5 cc. aniline and 5 cc. crude acetyl chloride (§ 34); note violence of action, and solidification of product; recrystallise without distilling. *Hydrolysis*.—Boil 2 grams with 20 cc. concentrated hydrochloric acid gently for a few minutes; then dilute, add caustic soda powder until strongly alkaline, and steam distil; test aniline. Distil 1 gram with 20 cc. water and 5 cc. concentrated sulphuric acid, and prove distillate contains acetic acid.

[251. *Thiocetanilide*.—Boil 12 cc. aniline, 8 cc. carbon disulphide, 20 cc. spirit and 4 grams powdered caustic soda, in a reflux apparatus, on a water-bath for four hours. Distil off alcohol and excess of disulphide, and proceed as directed. Take m.p. Yield 75 per cent.]

[252. *Sulphanilic Acid*.—Add slowly 15 cc. pure, recently distilled aniline to 30 cc. concentrated sulphuric acid, shaking the flask vigorously, proceed as directed, draining at pump. Recrystallise from hot water. Yield 60 per cent.]

## CHAPTER XLV

254. *Qualitative Tests for Phenol.*—Soluble in caustic soda, liberated by any acid: add dilute soda, shake with 10 cc. ether, pour off and evaporate 1 cc., note no residue; then acidify with dilute sulphuric acid, without removing ether, shake, remove and evaporate ether—oily residue of phenol, which test. Odour. Tribromophenol, and reversion. Blue with ferric chloride. Liebermann's blue: crystal of sodium nitrite to sulphonic acid (§ 250). Picric acid: warm with concentrated nitro-sulphuric acid, pour into water; yellow, darkened by alkali.

[254. *Anisole.*—Dissolve 1 gram clean sodium (in small pieces) in 25cc. methyl alcohol (in a reflux apparatus); add 4 grams phenol and 3 cc. methyl iodide, and boil on water bath until only slightly alkaline (about 2 hours) Distil off alcohol on water-bath, and pour the product into a little water; then make alkaline with caustic soda, and shake, to dissolve unchanged phenol. Separate oil (wash-liquor extracted with ether gives a further quantity), and distil from test tube. Note odour. Yield 80 per cent.]

255. *Phenol from Benzene-Sulphonate.*—Fuse 8 grams sulphonate with 20 grams caustic potash and 2 cc. water, stirring well with thick iron wire. Thermometer bulb must be protected with silver or steel cap, or else placed in sand under dish. Distil phenol from test tube after removing ether. Crystallise. Test. Yield 60 per cent.

255. *Phenol from Aniline.*—Add 9 cc. aniline to 10 cc. sulphuric acid in 140 cc. water; then 8 grams sodium nitrite in 20 cc. water until iodide-paper is blue (§ 260). Prove nitrogen. Steam distil and test. Yield 75 per cent.

[256. *Phenyl Isothiocyanate.*—Heat 1 gram thiocarbonyl (§ 251) with 5 cc. concentrated hydrochloric acid on a water-bath for an hour (in test tube). Distil to half bulk, pour into 50 cc. water, and distil the whole rapidly over a flame. The mustard oil passes over with the steam. Note odour. Extract distillate with ether; add a few drops of aniline, evaporate ether, warm, and stir; crystalline thiocarbonyl is left.]

## CHAPTER XLVI

[258. 260. *Benzene-diazonium Nitrate.*—Add 10 cc. aniline to cold mixture of 8 cc. concentrated nitric acid and 15 cc. water. Drain crystalline mass, and wash twice with 10 cc. cold water (until only slightly acid). Trioxide from 25 grams white arsenic (lumps, not powder, with 15 cc. concentrated nitric acid and 9 cc. water; warmed on water-bath at 70°; gas through empty bottle to deposit acid spray). Keep aniline paste ice-cold. Diazonium crystals may not appear at once; so keep in ice, and wait two hours before repeating (stir occasionally). Decompose with water (note yellow nitrophenol on steam distillation); hydrochloric acid; potassium iodide. Explode a little (dry a few milligrams on iron plate and hit with hammer).]

[258, 260. *Benzenediazonium Sulphate*.—Dissolve 15 cc. aniline in a solution of 20 cc. concentrated sulphuric acid in 180 cc. dry spirit; cool to 20°, and drop in slowly 22 cc. amyl nitrite (§ 230), shaking constantly, and keeping at about 20°. Proceed as directed, draining at pump. The sulphate is much less dangerous than the nitrate, but *should not be allowed to become dry*. Divide into three portions, two of which convert into phenol and iodo-benzene as directed (steam distil these). Dissolve the remainder in a little cold water and add to aqueous solutions of aniline, sodium phenate (part of diazonium solution previously heated, made alkaline, and cooled), and sodium 8-naphthol (§ 371); note coloured *anilide* (§ 259) and azo-compounds (§§ 382, 383).]

260. *Bromobenzene from Aniline by Diazonium Interaction* (Sandmeyer's method).—Boil a solution of 7 grams copper sulphate and 20 grams potassium bromide in 40 cc. water, with 11 grams of copper turnings and 3 cc. concentrated sulphuric acid, until colourless (reflux apparatus). Now add to the cuprous bromide 5 cc. of aniline, and then slowly (down the condenser), while still nearly boiling, a cold solution of 4 grams sodium nitrite in 15 cc. water. Steam distil and dry product. Compare with former products. Yield 70 per cent. Keep.

260. *Bromobenzene from Aniline by Diazonium Interaction* (Gatterman's method).—Dissolve 5 cc. aniline in the hydrobromic acid from the bromobenzene (§ 244), diluted to 60 cc. Cool, and add the nitrite solution (5 grams in 10 cc. water), slowly at first and towards end. (Take 1 drop of product for each test, and *dilute it with water* before placing on the iodide-paper, § 55; if the blue colour shows when only part of the nitrite has been added, wait, and test again, as the reaction is sometimes slow; if the blue colour cannot be obtained, even at the end, or the diazotised solution is turbid, add a little more dilute sulphuric acid). Add gradually to the diazotised solution, moist precipitated copper\* from 5 grams zinc dust and 20 grams copper sulphate. (Add the zinc-dust to the aqueous solution of the sulphate—it becomes very hot, and eventually colourless; wash the precipitated copper with water, stir with dilute hydrochloric acid until excess of zinc is dissolved, and effervescence ceases, wash again with water, and use at once.) When the reaction is over, steam distil and dry. Compare the product with the bromination product. B.p.; sp.gr. Yield 75 per cent. Keep.

260. *Elimination of Amino-Group from Aniline*.—Mix 7 cc. aniline with 15 cc. concentrated hydrochloric acid and 50 cc. water; keeping ice-cold. Diazotise crystalline magma with nitrite as before (6 grams in 14 cc.), and pour into an ice-cold solution of 10 grams caustic soda crystals in 30 cc. water, keeping ice-cold. Pour this product *gradually* down the condenser of a reflux apparatus, containing, at the ordinary temperature, a solution of 25 grams stannous chloride in 50 cc. water, to which a solution of 20 grams caustic soda in 20 cc. water has been added until the precipitate has practically redissolved (*keep cool*). When the evolution of nitrogen ceases, distil the benzene with steam, shake with dilute acid, dry and redistil. Note odour, b.p. and m.p. Nitrate a few drops (§ 292). Yield 80 per cent.

261. *Phenyldiazine* (Meyer's method).—Diazotise an ice-cold paste of 10 cc. aniline and 120 cc. concentrated hydrochloric acid with a solution of 10 grams sodium nitrite in 12 cc. water (not all of this should be required; test on *diluted* drops), and add an ice-cold solution of 50 grams stannous chloride in 60 cc. concentrated hydrochloric acid. Keep cool;

wait half an hour before filtering. Soda, 120 grams in 150 cc. water. Note b.p. and m.p. of hydrazine. Yield 80 per cent. Convert into glucosazone (§ 185) and benzene (below). Boil two or three drops with alkaline copper tartrate; note nitrogen and red oxide.

261. *Phenylhydrazine* (Fischer's method).—Diazotise a cold magma of 20 cc. aniline in 50 cc. concentrated hydrochloric acid as above (20 grams sodium nitrite in 80 cc. water; nearly all should be required), and then add this to solution of 30 grams crystallised sodium sulphite in the minimal amount of water (about 50 cc.). Heat the product to boiling, and add gradually 50 grams of zinc dust, with enough acetic acid to keep the solution acid; the dark green solution becomes colourless. Filter, boil down to half volume, add one-third volume of concentrated hydrochloric acid, and boil down until a sample crystallises on cooling. Crystallise out hydrazine hydrochloride, and treat as above. Yield 70 per cent.

261. *Reduction of Phenyl-hydrazine to Benzene*.—Run solution of 4 grams hydrazine in 4 cc. glacial acetic acid and 25 cc. water, into copper sulphate solution (20 grams in 60 cc.), boiling in reflux apparatus. Note evolution of nitrogen (prove), and deposition of metallic copper; distil off benzene with steam. Yield 70 per cent. Identify by odour, and conversion into nitrobenzene (odour) and dinitrobenzene (m.p.). Repeat, using hydrochloric acid, and isolate *chlorobenzene*.

## CHAPTER XLVI

[263. *Phenylhydroxylamine*.—To an emulsion of 10 cc. fresh nitrobenzene in a solution of ammonium chloride (6 grams in 100 cc. water) add *gradually*, with *continuous shaking* (or mechanical stirring), 20 grams of zinc dust, keeping the temperature (by cooling) *as nearly 15° as possible*; this should occupy an hour. Filter at pump, and proceed as directed (about 50 grams salt required; the base soon crystallises out). Yield 60 per cent. Note irritating odour. Recrystallise a little from benzene and take m.p. Note reduction of cold ammonio-silver and alkaline copper solutions.]

[263. *Nitrosobenzene*.—Dissolve 3 grams phenylhydroxylamine in dilute sulphuric acid (12 cc. in 200 cc. water), and add at once an ice-cold solution of 3 grams potassium dichromate in 150 cc. water. Distil with steam; the distillation is very rapid, and if the solid collects in the condenser, stop the water supply, or run steam through the jacket. Pour off water, and dry on a porous plate. Note odour and take m.p., noting colour when melted (or dissolved). Warm a crystal with hydrogen peroxide and caustic soda, and note odour of nitrobenzene. Warm remainder with aniline (1 mol.) in glacial acetic acid, and keep orange azobenzene for § 38c.]

[264. *Iodobenzene*.—Mix overnight a cold diazotised solution of 7 cc. aniline (see Elimination, § 260) with a solution of 18 grams potassium iodide in 30 cc. water; keep in a loosely-corked flask overnight, at the ordinary temperature, and next day, after warming until effervescence ceases, make slightly alkaline with soda, and distil the *iodobenzene* with steam. Separate, and dry with a fragment of calcium chloride. Dissolve the clear, dry *iodobenzene* (5 to 6 cc.) in 5 cc. dry chloroform, cool in ice, and saturate with chlorine; drain the yellow *iodochloride* on a porous plate. (Warm a crystal



in a test tube, and note dissociation to iodobenzene and chlorine.) Place the iodochloride in flask with caustic soda (half weight of soda in 10 parts of water), and keep alkaline (at the ordinary temperature) until colourless. Next day wash iodosobenzene with water, and dry on porous plate. Note action of heat and hydriodic acid (potassium iodide and sulphuric acid).]

## CHAPTER XLVIII

267. *Conversion of Benzoic Acid into Benzene*.—Distil an intimately ground mixture of 5 grams benzoic acid, 5 grams soda lime, and 5 grams fine iron filings from a test tube, heating from front backwards. Identify benzene by nitration (§§ 246, 292), odour and flame. Yield 50 per cent.

268. *Benzonitrile from Aniline*.—Diazotise 10 cc. aniline as in elimination of amino-group (§ 260, using proportionate quantities), and pour slowly down condenser of reflux apparatus, containing nearly boiling cuprous solution. (This as in § 124, with double quantities of water, and adding copper to cyanide solution until white precipitate just ceases to redissolve.) When all the diazotised solution has been added, distil with steam. There is no need to dry, as the nitrile is wanted for the next experiment. Note odour. Yield 60 per cent.

267. *Benzoic Acid from Benzonitrile*.—Make up steam distillate to 25 cc. with water, and boil in a reflux apparatus with 10 grams caustic soda. When no more ammonia is evolved, acidify cautiously with hydrochloric acid, and dry and sublime the precipitated benzoic acid. (Two watch-glasses, clamped edge to edge, with filter paper diaphragm; support on circular aperture in card resting on gauze, and heat with very small flame, cooling upper glass with moist pad of filter paper.) Yield 80 per cent. Take m.p. by capillary tube method. Test. Compare with stock.

[267. *Benzoic Acid from Bromobenzene*.—Dissolve 1½ grams bright magnesium ribbon in a solution of 5 cc. dry bromobenzene (or iodobenzene) in 10 cc. dry ether (§ 45; the action is slower than with alkyl iodides), and saturate with pure, dry carbon dioxide (§ 45). Distil off the ether, add water cautiously to the residue, and distil off any unchanged bromobenzene with steam; acidify the hot solution with dilute sulphuric acid, and allow the benzoic acid to crystallise. Sublime and determine m.p.]

268. *Qualitative Tests for Benzoic Acid*.—Ferric chloride in neutral solution, buff precipitate, which dissolves in a few drops of warm concentrated hydrochloric acid, and deposits acid on cooling. Odour of acid. Smoky flame. Benzene with soda-lime (nitrate).

268. *Ethyl Benzoate*.—Boil 5 grams benzoic acid with 20 cc. dry alcohol and 1½ cc. concentrated hydrochloric (or 1 cc. sulphuric) acid, in a reflux apparatus, until a few drops diluted with water give oil, without crystals (about two hours). Distil off excess of alcohol on water-bath, add water, neutralise acid with dilute soda. Separate oil, and distil from test-tube (§ 19), rejecting first portion (cloudy with water). Note odour. *Hydrolysis*.—Boil with half weight of caustic soda in twice weight of water (small flask with reflux tube); distil off alcohol (test); acidify residue with hydrochloric acid, and crystallise benzoic acid.

268. *Benzoyl Chloride*.—Powder 5 grams acid, 9 grams pentachloride

(good draught). Distil from test tube (Fig. 5). Redistil, noting b.p. and odour. Try action of cold and hot water on two or three drops, and then add caustic soda; prove benzoate and chloride. Yield 70 per cent.

270. *Benzoylating Alcohols, Phenols and Amines.*—*Ethyl benzoate*: 1 cc. chloride, 2 cc. spirit, soda until alkaline, warm (add more soda if necessary, and so on until permanently alkaline); pour into water; note odour. *Tribenzoyl-glycerol*: 5 drops glycerol, 1 cc. chloride, soda until alkaline; purify and recrystallise from spirit; take m.p. *Phenyl benzoate*: 1 gram phenol in dilute soda (excess), 1 cc. chloride; shake until odour of chloride has gone; pour off from oily product, wash with a little water, rub until crystalline; dry on filter paper; take m.p. *Benzanilide*: 1 cc. aniline, 1 cc. chloride, add soda (warming) until permanently alkaline; wash with water; crystallise from spirit; take m.p.

271. *Benzamide*.—Rest of chloride with powdered ammonium carbonate (1½ grams per cc.); warm on water-bath until odour of chloride has gone. Shake cold product with small quantities of cold water, to remove excess of carbonate; recrystallise from hot water. Take m.p. Yield 50 per cent. Hydrolyse with caustic soda, and prove ammonia and benzoate.

271. *Qualitative Tests for Hippuric Acid*.—Ferric chloride in neutral solution, brown flocculent precipitate. With soda lime, benzene (nitrate this) and ammonia (use well-washed ferric salt).

[272. *Acetophenone*.—Place in a dry reflux apparatus 7 grams resublimed aluminium chloride, covered with 20 cc. dry carbon disulphide, and add slowly through the condenser, keeping cool, a mixture of 14 cc. dry benzene and 10 cc. acetyl chloride. After an hour, add water slowly in the same way, and when there is no further action, distil off the carbon disulphide from a water-bath (no flame); wash the residual oil with dilute acid and water. (Alternative method: Distil 20 grams barium benzoate and 13 grams acetate, mixed as in § 88; avoid overheating benzoate in drying).

In either case fractionate product to separate benzene, noting odour and high b.p. Shake a little with phenylhydrazine acetate, and note *hydrazone*. Oxidise 1 gram with permanganate, as with acetone, and identify carbon dioxide and benzoic acid.]

[272. *Acetophenone-oxime*: *Acetanilide*.—Small reflux apparatus: 3½ grams hydrochloride in 5 cc. water, with 2 grams soda in 2 cc. water, and 6 grams acetophenone in 10 cc. spirit; if not clear on warming, add a little more spirit. Proceed as directed: 40 cc. water, saturate with salt before extracting with ether. Yield 80 per cent. Take m.p.

Beckmann transformation: As directed: 1½ grams powdered oxime, 20 cc. dry ether (§ 26), 3 grams powdered pentachloride. Take m.p.]

## CHAPTER XLIX

[273. *Saccharin*.—See § 314.]

275. *Benzaldehyde from Benzoic Acid*.—Distil 5 grams barium benzoate mixed with 2 grams barium formate, as in reduction of acetic acid, § 82. Note silver and rosaniline reactions, but not Fehling; *hydrazone*—2 or 3 drops distillate, same quantity phenylhydrazine, dissolved in glacial acetic acid and diluted; *bisulphite*—saturated solution of metabisulphite, as with acetone, § 89.

275. *Oxidation of Benzaldehyde to Benzoic Acid*.—Boil 3 cc. commercial benzaldehyde with 10 grams bichromate and 5 cc. concentrated sulphuric acid, in 50 cc. water. Cool, filter off benzoic acid and dry on plate; then dissolve in dilute caustic soda, filter, and reprecipitate with hydrochloric acid. Sublime and test.

[274. *Benzaldehyde from Benzyl Chloride or Bromide*.—Boil 7 cc. benzyl chloride or bromide (§ 280) with 6 grams copper nitrate in 60 cc. water, in a distilling-flask furnished with reflux condenser, passing a slow stream of washed carbon dioxide through the side-tube (directed upwards). When, after some hours, the product ceases to smell of the benzyl compound, distil the benzaldehyde with steam, and extract with ether (saturate the water with salt). Test as above.]

276. *Condensation of Benzaldehyde with Acetone*.—Warm 2 cc. benzaldehyde with 4 cc. acetone and 10 drops caustic soda, diluted with 50 cc. water in a beaker of boiling water for an hour; the product crystallises when cold, recrystallise from water. Note m.p.

## CHAPTER L

[279. *Separation of Toluene from Commercial Product*.—As with benzene, using "light oil fraction" (§ 243), or commercial "toluol."]

[279. *Synthesis of Toluene from Bromobenzene*.—Boil 7 grams *clean* sodium gently with 50 cc. dry ether, in reflux apparatus on water-bath (good condensation), until hydrogen bubbles cease to rise. Then cool, and add slowly through condenser, a dry mixture of 10 cc. bromobenzene, 7 cc. methyl iodide, and 5 drops dry ethyl acetate. \*Reaction must take place *quietly*. Next day, pour from solid, distil off ether on water-bath, and then toluene over gauze. Note b.p. Prove sodium bromide.]

280. *Benzyl Bromide*.—Boil 20 cc. toluene with 10 cc. bromine in bright daylight, until no more hydrogen bromide is evolved—several hours (collect gas as with bromacetic acid). Pour product into cold water; wash oil with dilute caustic soda until colourless; dry and fractionate (210°). Yield 60 per cent.

[280. *Benzyl Chloride*.—In sunlight or bright daylight until proper increase of weight is obtained (weigh whole apparatus: 4 grams for each 13 cc. toluene); proceed as with bromide.]

280. *Oxidation of Benzyl Bromide to Benzoic Acid*.—Boil half product in reflux apparatus with 10 cc. nitric acid and 40 cc. water, until dissolved, and prove benzoic and hydrobromic acids.

280. *Hydrolysis of Benzyl Bromide*.—Boil 5 cc. benzyl bromide (or chloride) with 7 grams sodium carbonate (dry) and 70 cc. water, in a reflux apparatus, until the odour of the halide is no longer perceptible (several hours). Cool, extract the benzyl alcohol with ether, and after distilling off the ether (§ 249), distil from a test-tube. Note odour. Prepare benzoyl derivative (§ 270). Oxidise a few drops to benzoic acid by boiling with nitric acid, and to benzaldehyde by boiling with acid chromate.

280. *Benzyl Alcohol and Benzoic Acid from Benzaldehyde*.—Shake vigorously 7 cc. aldehyde with 5 grams caustic soda in 5 cc. water; distil ether from a water-bath, and precipitate benzoic acid from the aqueous solution with hydrochloric acid.

[282. *Mandelonitrile and Mandelic Acid*.—Dissolve 10 grams sodium metabisulphite in 40 cc. warm water, and cool; add, with much shaking, 10 cc. benzaldehyde, and cool; finally, add to the paste 6 grams 98 per cent. potassium cyanide in 15 cc. water. Separate the nitrile with a tap-funnel (boil a few drops with strong caustic soda, and note benzaldehyde and sodium cyanide). Boil the nitrile with concentrated hydrochloric acid (4 vols.) until dissolved; evaporate to dryness on water-bath, and extract mandelic acid with dry alcohol. Take m.p. Benzoylate.]

## CHAPTER LIII

292. *Metadinitrobenzene*.—As with nitrobenzene, but add the benzene to the acid mixture drop by drop, shaking well and allowing to heat. Finally boil for 15 minutes on sand-bath. Pour into a large quantity of water (litre), filter at pump, wash with water until free from acid, and recrystallise from dilute alcohol (§ 244). Take m.p. Yield 85 per cent.

[292. *Symmetrical Trinitrobenzene*.—Add 5 grams powdered *m*-dinitrobenzene to a mixture of 10 cc. fuming nitric acid (sp.gr. 1.5) and 15 cc. Nordhausen sulphuric acid. Heat on water-bath about 2 days (flask with plain reflux tube), and finally for an hour at 120–130°. Isolate as with dinitrobenzene. Take m.p.]

293. *Metanitraniline and Metanitrophenol*.—Dissolve 10 grams dinitrobenzene in 35 cc. spirit; add 6 cc. 880 ammonia, and pass washed hydrogen sulphide until weight increases by 6 grams. Proceed as directed, extracting solid with warm dilute hydrochloric acid until a sample of extract ceases to precipitate with ammonia. Note m.p. Convert portion into metanitrophenol, as aniline into phenol, and note nitrogen; take m.p.

293. *Ortho- and Para-Nitracetanilide*.—Add 10 grams powdered anilide to 25 cc. red nitric acid (sp.gr. 1.5), proceeding as directed; shake with portions of 4 cc. cold chloroform 5 times, filtering through small filter each time. Recrystallise, and note colour and m.p. *Ortho- and Para-Nitraniline*.—Boil with acid until dissolved, then proceeding as directed, and recrystallising from spirit. Note colours and m.p.; *p*-compound is not volatile with steam, and gives a lemon-yellow dichloro-compound with chlorine water; *o*-compound is volatile with steam.

294. *Nitrophenols—Ortho and Para-Compounds*.—Add 10 grams of phenol slowly to 15 cc. concentrated nitric acid in 50 cc. water at 30°, with much shaking; allow to cool, keep overnight, and proceed as directed. The para-compound may require decolorising with animal charcoal (in hot water), or it may be extracted with hot concentrated hydrochloric acid. Note m.p. and properties. Make sodium salts with carbonate (note carbon dioxide), and recrystallise. Note colours. *Meta-Compound*.—Convert portion of *m*-nitraniline as aniline into phenol, using concentrated solutions. Make product alkaline, extract impurities with ether, then acidify and extract the nitrophenol. Take m.p.

295. *Picric Acid*.—Dissolve 10 grams phenol in 7 cc. concentrated sulphuric acid; dilute solution with 8 cc. water, cool, and add slowly to 30 cc. fuming nitric acid, shaking well. Heat on water-bath until yellowish.

Pour into water and proceed as directed. Note m.p. Make sodium salt (note carbon dioxide). Note colourless solution in paraffin.

[295. *Picric Acid from Trinitrobenzene*.—Heat 1 gram powdered s-trinitrobenzene (§292), on a water-bath, with  $1\frac{1}{2}$  grams potassium ferricyanide and 1 gram caustic soda in 20 cc. water, until dissolved. Filter, if necessary, precipitate picric acid with sulphuric acid, and recrystallise. Take m.p. Test for ferrocyanide in filtrate.]

[296. *Metaphenylen-Diamine*.—Add 20 grams powdered dinitrobenzene slowly, with constant stirring, to 60 grams reduced iron suspended in 3 cc. glacial acetic acid and 60 cc. water. Proceed as directed. Yield 50 per cent.]

## CHAPTER LV

302. *Resorcinol*.—Heat 10 grams sodium benzenesulphonate with 20 cc. fuming sulphuric acid, in a reflux apparatus on a sand-bath, for 2 hours. Isolate the sodium disulphonate (with unchanged monosulphonate) by calcium carbonate method. Fuse the mixed sulphonates with potash (§255), and separate phenol by distillation with steam. Extract resorcinol with ether. Note m.p., ferric colour, and bromine precipitate. Yield 40 per cent.

303, 304. *Quinol and Quinone*.—Add 12 grams powdered dichromate (or 14 grams sodium salt in 25 or 30 cc. water), in small quantities, to 10 cc. aniline, dissolved in 50 cc. concentrated sulphuric acid with 250 cc. water, ice-cooled; stir well, and keep cool. After a night at the ordinary temperature, cool again, and add 24 grams dichromate (or 28 grams sodium salt) in the same way. After 3 hours, extract; three extractions with 50 cc. ether. Distil off ether on water-bath; residue with steam. Yield 30 per cent. (Or better, reduce brownish, turbid product with 20 grams metabisulphite and 10 cc. sulphuric acid, and when practically colourless, extract quinol with ether; then oxidise ether-free product with dichromate and sulphuric acid, distilling with steam. Yield of quinol 80 per cent; of quinone 70 per cent. Note action of ferric chloride on quinol.) Note m.p., colour, volatility, odour.

[305. *Phloroglucinol*.—Fuse 5 grams resorcinol (or phenol) with 30 grams caustic soda and 3 cc. water (with phenol, heat until layer of phenate disappears, and the whole is somewhat spongy). Yield 60 or 30 per cent. Note m.p. and ferric chloride colour.]

*Pyrogallol*.—Heat gallic acid to its m.p. in test tube. Note carbon dioxide and sublimed pyrogallol. M.p. of latter, and colour with iron salts. Absorption of oxygen from air by its solution in caustic alkali (invert empty test-tube in a wider test-tube, containing 1 gram pyrogallol in a cold solution of 8 grams potash in 10 cc. water).

## CHAPTER LVI

308. *Salicylic Acid*.—Dissolve  $4\frac{1}{2}$  grams caustic soda in 6 cc. water in iron dish; add 10 grams phenol; heat gently and stir vigorously until powder is obtained—not cake. Powder again quickly (it should be quite

dusty), place *while still warm* in a dry distilling flask, and pass *washed and dried* carbon dioxide (§ 45), raising temperature gradually from 100° to 200°—oil bath, 2 hours. Yield 50 per cent. Recrystallise acid from water; note m.p. and tests. *Qualitative Tests*.—Violet with ferric chloride in neutral solution, not changed by acetic acid; flocculent tribromo-compound; intimate mixture with lime gives phenol (odour: picric acid).

308. *Salicylic Aldehyde*.—Dissolve 12 grams phenol in a solution of 30 grams caustic soda in 40 cc. water, warm in reflux apparatus on water-bath (about 50°), and add slowly (over half an hour) 15 cc. chloroform. Boil the reddish product for half an hour on a water-bath, distil off the chloroform, and the acidified residue with steam (the floating oil passes over). Dissolve 12 grams metabisulphite in the distillate; cool, and extract the phenol with 20 cc. ether (twice, saturating with salt); now acidify with sulphuric acid, drive off the sulphur dioxide, cool, and extract the aldehyde with ether. Distil off the ether (§ 249), and redistil the aldehyde from a test-tube. Note odour, ferric colour, action on skin, and aldehyde tests. Filter residue from steam distillation, and extract with ether as before; distil off ether, and crystallise residual *parahydroxy-aldehyde* from a little water. Yields 40 and 10 per cent.

311. *Qualitative Tests*.—*Gallic Acid*: Blue-black with ferric or ferrosulfuric salts. No precipitate with gelatine. Rufigallic acid—moisten solid with concentrated sulphuric acid on watch-glass, warm till red, turn into cold water. *Tannin*.—Blue-black with iron salts. Precipitate with *cold, fresh* gelatine solution (soak fragment of gelatine in cold water until it swells, then warm with a little water). Rufigallic acid, as with gallic acid.

## CHAPTER LVII

314. *Toluene-Sulphonic Acids*.—Mixed *o*- and *p*-compounds in same way as with benzene, but more easily; convert into mixed *acid chlorides* and *amides* (§ 247). *Saccharin*.—Add permanganate solution (1 gram in 20 cc. water) to a boiling solution of the mixed amides (1 gram) as long as the permanganate is reduced; filter from manganese dioxide, evaporate to dryness, and note intensely sweet taste of product.

315. *Cresols*.—Mixed *o*- and *p*-compounds as with phenol; *para-compound* from commercial *p*-toluidine in the same way as phenol from aniline.

316, 317. *Nitrotoluenes and Toluidines*.—Mixed *o*- and *p*-compounds, in the same way as nitrobenzene and aniline.

## CHAPTER LVIII

321. *Paratolusic Acid from Paratoluidine* (commercial).—Precisely as with benzoic acid from aniline. The nitrile may also be hydrolysed by boiling in a reflux apparatus with moderately concentrated sulphuric acid (6 cc. acid and 2 cc. water per gram); the acid separates on pouring the product into water. Note m.p. and reactions (as benzoic acid).

322. *Mixed Xylenes*.—Fractionate 50 cc. commercial xylene ("xylol"), isolating fraction about 135–140°. Sulphonate and nitrate small quantities.

[322. *Paraxylene*.—Distil 20 grams camphor with 20 grams crushed zinc chloride. Warm product with concentrated sulphuric acid (not easily sulphonated); wash with alkali and water; dry and fractionate. Note b.p.]

324. *Phthalic Acid and Anhydride*.—Mix 6 grams naphthalene and 11 grams potassium chlorate (powdered separately), into small pellets with a little water, and add these one by one to 40 cc. concentrated hydrochloric acid (draught cupboard). Add to the washed, pasty chloride (in reflux apparatus), in small portions, a mixture of 2 cc. ordinary and 1 cc. fuming nitric acid per gram, heating on a sand-bath until dissolved; boil down (still in draught) until a sample of residue (phthalic acid) crystallises on cooling; and then either recrystallise from water, or distil to dryness (test-tube with plain condenser) and reconvert anhydride into acid (dissolve in alkali, and precipitate). Note m.p. of acid and anhydride, and interconvertibility. Yield 50 per cent.

324. *Phthalic Acid to Benzene*.—Mix 1 gram with 10 grams powdered lime and 2 grams iron filings. Prove benzene by nitration.

325. *Oxidation of Paratoluic to Terephthalic Acid*.—Dissolve 3 grams acid with 2 grams caustic soda in 240 cc. water; add slowly, to boiling solution, 11 grams permanganate in 440 cc. water, until permanently pink. Wash and dry terephthalic acid, noting insolubility. Sublime.

326. *Dihydroterephthalic Acid*.—Dissolve 1 gram terephthalic acid in a little dilute soda (note that a few drops of the solution have no action on cold, dilute alkaline permanganate). Dilute the solution to 50 cc. and add 3½ per cent. sodium amalgam (5 grams sodium in 10 cc. mercury), in small quantities, until hydrogen is evolved freely (use small flask with loose cork, and do not allow to become hot). Acidify product with dilute sulphuric acid, filter, extract dihydro-acid, with ether, and evaporate. Note action of acid on bromine water and cold alkaline permanganate.

## CHAPTER LIX

328. *Mesitylene*.—Mix 50 cc. acetone, in 50 grams clean sand, with 65 cc. acid, diluted with 20 cc. water; next day distil from sand-bath. Note bromination, nitration and sulphonation (on a few drops in test-tube). Oxidise as directed to mesitylenic and uvitic acids, and note m.p.

## CHAPTER LX

332. *Cinnamic Acid*.—Boil 10 cc. benzaldehyde and 14 cc. acetic anhydride—both freshly distilled—with 5 grams powdered, recently fused sodium acetate (flask with air-condenser), 6 hours on sand-bath; if possible the boiling should not be interrupted, and in any case the upper end of the reflux tube should be guarded by a calcium chloride tube. Mix the molten product with water, steam distil, and recrystallise; animal charcoal, 5 grams. Yield 50 per cent. Note m.p., action of bromine water.

alkalies, and permanganate; yellow precipitate with ferric chloride.

334. *Styrene from Cinnamic Acid*.—Distil 1 gram cinnamic acid with 2 grams soda-lime, and redistil distillate with steam; note action of bromine water and alkaline permanganate.

337. *Aniline from Indigo*.—Distil 2 grams indigo from flared-glass test tube with 4 grams caustic soda and 1 cc. water. Prove aniline by tests.

## CHAPTER LXI

340. *Pinene*.—Distil some ordinary spirit of turpentine with steam. Saturate some with dry hydrogen chloride gas. Shake some with permanganate solution, and with bromine water.

[340. *Carvacrol and Cymene*.—Distil 24 grams camphor with 5 grams iodine, and fractionate. Note b.p. Distil crude carvacrol with phosphorus pentasulphide (warm red phosphorus with sulphur in dish; theoretical quantities); oxidise cymene with dilute nitric acid, and identify terephthalic acid. Also distil 10 grams camphor with same weight pentoxide; redistil cymene, and note b.p. and characters.]

341. *a-Bromocamphor*.—Warm 7 grams camphor (crushed into small pieces) with 3 cc. bromine in a small reflux apparatus (with water trap). When the violent action ceases, heat to 135° (oil-bath), wash with dilute soda, and crystallise from spirit. Note inaction of bromine water and alkaline permanganate (also on camphor).

[342. *Camphoric Acid*.—Heat 20 grams camphor in long-necked flask on water-bath, with 180 cc. concentrated nitric acid and 90 cc. water, until nitrous fumes nearly cease (3 or 4 days). Boil down to incipient crystallisation, cool, and dry crystals on plate; dissolve in soda, reprecipitate with hydrochloric acid, and recrystallise from water. Yield 40 per cent.]

## CHAPTER LXIII

[353. *Diphenyl*.—Drop benzene from a tap-funnel (15–25 drops per minute) into the turned-up end of a long iron gas pipe, filled with pumice, and heat in a combustion furnace to dull redness. Yield 50 per cent. of benzene unrecovered. Fractionate with air condenser, recrystallise, and note m.p.]

355. *Benzoin*.—Dissolve 10 cc. benzaldehyde in 30 cc. spirit; add 2 grams 98 per cent. cyanide in 10 cc. water; heat on water-bath (reflux) for an hour, and allow to crystallise. Recrystallise from alcohol, and note m.p. Yield 80 per cent. Note reduces Fehling.

356. *Benzil*.—Heat 5 grams crude benzoin with 10 cc. concentrated nitric acid and 2 cc. water, for 2 hours on a water-bath, shaking well. Pour into cold water, wash, and crystallise from spirit. Yield 80 per cent. Note m.p. and violet with alcoholic potash.



## CHAPTER LXIV

359. *Rosaniline*.—Heat 1 cc. aniline and 1 gram *p*-toluidine with 1 gram mercuric chloride. Note colour.

360. *Mordants*.—Soak a cotton rag in rosaniline solution, drain and dry; note colour is washed out by soap. Dip rag in dilute tannin solution and wring; then dip in dilute tartar emetic solution and wring; finally, dip in rosaniline. Note colour is now fast to soap. Repeat with sodium picrate and aluminium acetate (alum solution) to lead acetate solution, until all lead is precipitated; use clear filtrate).

361. *Colour Base and Leuco-Base*.—All following on few milligrams only. Decolorise magenta solution with concentrated hydrochloric acid, and restore colour with water. Precipitate white colour base with strong caustic soda, wash, and redissolve in dilute acid, noting restoration of colour. Reduce dye with dilute hydrochloric acid and zinc dust; add excess of caustic soda, and extract leuco-base with ether; distil off ether on water-bath, and warm residue with few drops of concentrated sulphuric acid; pour into water, and note dye.

[361. *Triphenylmethane*.—Add to 60 cc. benzene and 7 cc. chloroform, both perfectly dry, in dry reflux apparatus, 12 grams fresh, resublimed aluminium chloride in 6 portions. Boil for half an hour, and proceed as directed (vacuum distillation is convenient above 200°). Yield 40 per cent. Note m.p.]

[362. *Pararosaniline from Triphenylmethane*.—As directed: 2 grams hydrocarbon with 7 cc. fuming nitric acid; separate, wash and dry nitro-compound before reducing; to cc. acetic acid, and 2 grams zinc dust; when latter is in excess, hydrogen is evolved freely.]

## CHAPTER LXV

363. *Aniline Blue*.—Boil (gently) 1 gram rosaniline acetate with 10 cc. aniline, in a large test-tube provided with an air-cooled reflux tube; if the tube rests on a sand-bath, it can be left, once the flame has been regulated. After some hours, extract the cold product with dilute hydrochloric acid, filter, and evaporate to dryness. Extract the blue dye with spirit, and dye some wool.

[365. *Methylene Blue*.—Dissolve  $\frac{1}{2}$  gram paramino-dimethylaniline (§ 382) in 20 cc. water, with some dilute sulphuric acid, and keep as test. Mix two or three drops with same amount of dilute hydrochloric acid and ferric chloride solution; then trace of soluble sulphide gives an intense blue.]

[366. *Leuco-Malachite-Green*.—Heat 9 grams powdered, fused zinc chloride with 20 cc. dimethylaniline and 9 cc. benzaldehyde. After removing excess of aniline as directed, crystallise leuco-base from alcohol.]

[366. *Malachite Green*.—Dissolve 2 grams leuco-base in 100 cc. water with 2 cc. hydrochloric acid, 2 cc. glacial acetic acid. Stir in washed lead peroxide (just precipitated by excess of bleaching solution from solution of 3 grams lead acetate). Add sodium sulphate solution (6 grams in 30 cc.) until no more precipitate is formed; filter off lead sulphate and

chloride. Salt out with solution of 5 grams zinc chloride in 5 cc. water; dye mordanted cotton as in § 360.]

[367. *Phenol-Phthalein*.—Heat 5 grams phthalic anhydride, 9 grams phenol, and 4 cc. concentrated sulphuric acid on sand-bath for 4 hours (small flask, reflux tube). Proceed as directed.

367. *Colour Changes of Phenol-Phthalein*.—Dissolve 2 or 3 milligrams of phenol-phthalein, by shaking with a cold solution of 2 grams caustic soda in 8 cc. water; the initial red colour soon practically disappears. Dilute some of the solution and boil; the colour reappears, but again disappears on cooling. Add acetic acid drop by drop to some of the original solution until the pink vanishes abruptly, then add a drop or two of the original solution to restore the pink colour; the solution now contains only a slight excess of alkali (i.e. above 1 equivalent), and when diluted and boiled turns permanently deep red.

## CHAPTER LXVI

369. *Naphthalene*.—Distil 10 grams commercial naphthalene, 5 grams caustic soda, 100 cc. water with steam. Dry the distilled hydrocarbon, and sublime, as with benzoic acid (§ 267).

370. *Nitronaphthalene*.—Heat 10 grams naphthalene with 50 cc. glacial acetic acid and 10 cc. concentrated nitric acid, as directed; recrystallise washed product from alcohol. Note m.p. Yield 70 per cent.

370. *Naphthalene  $\beta$ -Sulphonic Acid*.—Heat 20 grams powdered naphthalene with 14 cc. concentrated sulphuric acid for 4 hours at 180°. Pour into 500 cc. water, filter off any naphthalene, and then as with ethyl sodium sulphate. Yield 80 per cent. on unrecovered hydrocarbon.

371.  *$\alpha$ -Naphthylamine*.—Dissolve 5 grams nitro-compound in 10 cc. glacial acetic acid, and add 7 grams iron filings; keep at 50° for 2 hours, then on water-bath for 1 hour. Filter, and proceed as with aniline (ferrous hydroxide does not redissolve). Compare with aniline.

371.  *$\beta$ -Naphthol*.—As with phenol: 5 grams sodium sulphate, 15 grams caustic potash, 1 cc. water; 200° for an hour, and finally 300° for a few minutes. Dissolve cold melt in 500 cc. hot water, and precipitate with dilute hydrochloric acid; recrystallise from hot water. Yield 60 per cent. Note m.p. Compare with phenol tests. Pass dry ammonia over melted  $\beta$ -naphthol, and isolate naphthylamine.

372. *Oxidation of Naphthalene to Phthalic Acid*.—See § 324.

373.  *$\alpha$ -Naphthoquinone*.—Add 9 grams chromic anhydride slowly to a warm solution of 3 grams naphthalene in 20 cc. glacial acetic acid. Boil gently for two minutes; dilute, filter, and distil the washed product with steam. Note m.p., colour and odour.

## CHAPTER LXVII

375. *Anthraquinone*.—To a boiling solution of 8 grams anthracene in 60 cc. glacial acetic acid, add cautiously 15 grams chromic anhydride in 10 cc. water and 30 cc. glacial acid. Precipitate product with water, wash, dry, and sublime. Note colour and m.p. Yield 80 per cent.

375. *Conversion of Anthraquinone into Benzoic Acid.*—Fuse 3 grams in iron spoon at 200° with 3 grams caustic soda and 1 cc. water; dissolve, melt in water, and precipitate benzoic acid with dilute hydrochloric acid; collect, wash, dry, and sublime. Identify by m.p. and tests.

[377. *Sodium Anthraquinone-Sulphonate.*—Heat 1 gram anthraquinone with 10 cc. crystallisable, fuming sulphuric acid until nearly dissolved; dilute, filter, and neutralise hot with sodium carbonate; the sodium salt crystallises on cooling. Yield 60 per cent. *Alizarin.*—Grind 2 grams sulphonate with 5 grams caustic soda,  $\frac{1}{2}$  gram potassium chlorate and 5 cc. water; heat in sealed hard-glass tube (one-third full) for 20 hours in boiling aniline. Extract alizarin with boiling water, and precipitate with dilute acid; wash, dry, and sublime. Yield 50 per cent. Note m.p., colour, solubility in caustic alkalies, and precipitation by metallic salts (alum, ferric chloride, chrome alum); note colours of lakes.]

## CHAPTER LXVIII

380. *Azoxybenzene.*—Dissolve 3 grams sodium in 40 cc. dry methyl alcohol; add 5 cc. nitrobenzene; proceed as directed. Note m.p. Yield 50 per cent. Distil some with fine iron filings (3 parts by weight), and compare azobenzene with that prepared by following method.

380. *Azobenzene.*—Boil 10 grams caustic soda with 50 cc. spirit (reflux) until nearly dissolved; cool, and add 10 cc. nitrobenzene. After 2 hours add cautiously 5 grams zinc dust, and boil for 10 hours. Distil off alcohol, extract residue with hot water and hot dilute hydrochloric acid (to remove zinc compound). Finally wash with water, and crystallise from boiling alcohol. Yield 70 per cent. Note m.p. and red vapour. Compare with product from nitrosobenzene, § 263.

380. *Hydrazobenzene and Benzidine.*—As with azobenzene, but continue addition of zinc dust until colourless; proceed as directed—the water should contain some sulphur dioxide. Take m.p.; oxidise alcoholic solution with nitrous fumes (§ 258), and collect azobenzene. Benzidine: Boil the hydrazobenzene with concentrated hydrochloric acid for a few minutes, pour into water, and add excess of caustic soda; drain, and re-crystallise from dilute spirit containing sulphurous acid. Take m.p.

381. *Amino-Azobenzene.*—Dissolve 5 grams aniline hydrochloride in 20 cc. aniline at 35°; add 2½ grams sodium nitrite in 4 cc. water; keep at 35–40° for 1½ hours; leave. Next day stir in 14 cc. concentrated hydrochloric acid (or more, if necessary), and proceed as directed.

[381. *Diazobenzene-Anilide and Amino-Azobenzene.*—Mix a solution of 4 cc. aniline in 10 cc. dry ether with 2 cc. amyl nitrite in 10 cc. ether, and evaporate in a flat dish over sulphuric acid. Golden yellow crystals of the anilide separate; drain, and dry on a porous plate. Mix at once with aniline (3 parts) and dry aniline hydrochloride ( $\frac{1}{2}$  part), and warm at 45°, until liquid. Next day dissolve in hydrochloric acid, and proceed as above.]

382. *Triamino-Azobenzene.*—A few drops of a dilute solution of metapenylenediamine salt to solution containing a trace of nitrite; can be used for the colorimetric estimation of nitrites in water.

[382. *Methyl Orange.*—Neutralise 5 grams sulphanilic acid (§ 252) with sodium carbonate (about 1½ grams in 50 cc. water), add 2 grams sodium

nitrite in 4 cc. water, cool with ice, and acidify (gradually) with  $3\frac{1}{2}$  cc. of concentrated hydrochloric acid, diluted with the same volume of water. Add to this diazotised solution, a cold solution of  $3\frac{1}{2}$  cc. dimethylaniline in dilute hydrochloric acid (3 cc. in 100 cc. water); make just alkaline with soda (red changes to yellow), and saturate solution with salt. Allow the methyl orange to separate; collect, and recrystallise from hot water.]

[382. *Constitution of Methyl Orange: p-Aminodimethylaniline.*—Add a solution of 5 grams granulated tin in 25 cc. hot concentrated hydrochloric acid, to 3 grams commercial methyl-orange dissolved in 10 cc. hot water. Boil gently for 15 minutes, and proceed as directed, isolating sulphanilic acid and aminodimethylaniline.]

## CHAPTER LXIX

386. *Quinoline.*—Mix 10 cc. nitrobenzene, 20 cc. aniline, 50 cc. glycerol; cautiously stir in 30 cc. concentrated sulphuric acid. After 3 hours heating on sand-bath (reflux) the nitrobenzene should have disappeared. Much soda is required (dissolve 50 grams crystals in 50 cc. water, and add cautiously, cooling, as in § 249). 1 gram nitrite should be enough. Yield 40 per cent. Note b.p., odour. Make hydrochloride and crystallise; warm with a few drops of methyl iodide. Note alkaloid tests (§ 399).

386. *Quinoline from Cinchonine.*—Distil 5 grams cinchonine from small hard-glass flask with 7 grams caustic soda powder and 4 cc. water; sand-bath, at as low a temperature as possible. Redistil quinoline with steam.

387. *Pyridine.*—Make and recrystallise pyridine sulphate from commercial product. Warm a few drops with methyl iodide; note explosive action, and yellow crystalline product. Note general alkaloid tests.

[388. *Piperidine.*—To a solution of 4 cc. pyridine in 30 cc. spirit, in a reflux apparatus, add gradually 10 grams of sliced sodium (keep in ether until wanted); more alcohol must be added as the ethoxide accumulates. Distil with steam, acidify with hydrochloric acid, and evaporate to dryness on a water-bath. Decompose piperidine hydrochloride with concentrated soda (compare odour with pyridine), extract with ether. Very alkaline; nitrosamine with nitrite; general alkaloid tests.]

## CHAPTER LXX

[392. *Collidine.*—Warm 20 cc. ethyl acetoacetate on a water-bath with 6 grams fresh aldehyde ammonia. Stir product into 10 cc. dilute hydrochloric acid, wash, dry on plate. Suspend in 20 cc. cold spirit, pass nitrous fumes (§ 258) until drop dissolves in dilute hydrochloric acid. Evaporate on water-bath, liberate collidine-ester with sodium carbonate, extract with ether. Hydrolyse ester with alcoholic potash (10 grams, 30 cc.; reflux, water-bath, 3 hours), drain and dry potassium carboxylate (insoluble in spirit). Distil with excess of lime, dry collidine (in ether) with potash, fractionate. Yield 70 per cent. at each stage. Compare with pyridine.]

## CHAPTER LXXI

399. *Qualitative Tests for Alkaloids in General*.—Phosphomolybdate (2 grams phosphomolybdic acid, 25 cc. water, and just enough caustic soda to dissolve to clear colourless solution); iodine in potassium iodide (2 grams iodine, 2 grams potassium iodide, 50 cc. water); potassium mercuriodide (1 gram mercuric chloride, 2 grams potassium iodide, 25 cc. water); tannin. Most alkaloids are bitter, soluble in dilute acids, and reprecipitated by ammonia. Apply tests to all alkaloids available; compare with quinoline and pyridine.

[399. *Estimation of Total Alkaloids in Cinchona Bark*.—The alkaloids are set free with lime, extracted with alcohol, converted into sulphates, purified; again set free with caustic soda, extracted with chloroform, and weighed after evaporating solvent.]

399. *Qualitative Tests*.—*Quinine*: Fluorescence with dilute sulphuric acid in dilute solution; very bitter; precipitated by ammonia; chlorine tests. *Cinchonine*: Soluble in acids, precipitated by ammonia; ferrocyanide from concentrated solution only.

## CHAPTER LXXII

402. *Qualitative Tests*.—*Strychnine*: Soluble in acids; precipitated by ammonia; dichromate crystal through solution in cold, concentrated sulphuric acid, violet; very bitter. *Brucine*: Soluble in acids, precipitated by ammonia; very bitter; red with nitric acid, changed to violet by stannous chloride. *Morphine*: Soluble in acids; blue with one or two drops of ferric chloride (faint; masked by meconic acid); iodine with iodic acid (turns chloroform purple); small crystal of ammonium molybdate to cold solution of dry alkaloid in concentrated sulphuric acid, fine blue colour.

402. *Extraction of Alkaloids from Organic Mixture*.—Extract with acid ether, followed by alkaline ether-chloroform as directed, using small quantities of solvent; evaporate ether-chloroform, and test residue.

[403. *Estimation of Morphine in Opium*.—The morphine is dissolved in lime-water, precipitated by ammonium chloride, impurities and extractive matter are dissolved out with alcohol, and the alkaloid precipitated in crystalline form from the aqueous solution by ether.]

## CHAPTER LXXIII

[406. *Thiophene*.—Shake 10 cc. commercial benzene with 10 cc. concentrated sulphuric acid, containing a small crystal of phenanthraquinone or isatin (which make). Note blue.]

406. *Dinitrothiophene*.—Make a little metadinitrobenzene from "50 per cent. benzol," and note red colour with alkali in pure alcohol (free from acetone). Compare with dinitrobenzene from pure benzene.

406. *Furfural*.—Distil 5 grams chopped straw with 10 cc. concentrated hydrochloric acid in 100 cc. water. Note odour of distillate; colour with aniline acetate; immediate precipitate with phenylhydrazine acetate.

## SUMMARY OF OPERATIONS AND AGENTS

(The numbers refer to pages.)

### PURIFICATION OF GASES AND VERY VOLATILE LIQUIDS.

*Fractional Condensation.*—Ethyl chloride, 23; aldehyde, 98; ethylene, 128.

*Washing.*—Dilute alkali, 23; sulphuric acid, 128; water, 23, 128.

*Drying.*—Sulphuric acid, 23; quicklime, 64; calcium chloride, 98.

*Conversion into Solid.*—Ethylamine, 64; aldehyde, 98; acetylene, 137.

### PURIFICATION OF LIQUIDS.

*Filtration and Mechanical Separation.*—Large quantities, 25; rapid, 25; molten solids, 316, 567, 572; tap-funnel, 19; capillary pipette, 565.

*Distillation.*—Moderate quantities, 4; large quantities, 7; small quantities, 18; reduced pressure, 184; with steam, 84, 315, 407, 205; liquids of high boiling-point, 317; fractional, 4, 6, 314, 323; destructive, 33.

*Salting Out.*—Caustic alkali (alcohols), 18, 167; calcium chloride (middle fatty acids, ketones, etc.), 49, 108; common salt (esters, soaps), 41, 53, 183.

*Extraction with Solvent Liquid.*—Ether (general), 103, 322; dilute acids (basic liquids), 521; alkalies (phenolic and acid liquids), 328.

*Washing.*—Water (general for insoluble liquids); dilute alkalies (haloid compounds, ethers, etc.), 19, 28, 129, 315; brine (soluble esters), 41; concentrated alkali (alcohols), 18, 167; concentrated sulphuric acid (saturated compounds), 85, 94.

*Drying.*—Calcium chloride (general for indifferent liquids), 19, 28, 107, 129; quicklime, caustic alkali (alcohols, amines), 7, 167, 322; anhydrous potassium carbonate (esters), 41; phosphorus pentoxide (esters, nitriles), 41, 63; metallic sodium (ethers), 28, 568; fractional distillation (liquids of high boiling-point), 315, 317.

### PURIFICATION OF SOLIDS.

*Crystallisation.*—From water (acids, salts, amides, amines, etc.), 25, 154, 323; alcohol (substances insoluble or too soluble in water), 218, 316, 567; acetone (various), 86, 149, 584; benzene, toluene (mainly aromatic compounds), 399, 503; petroleum (mainly aromatic compounds), 385; filtration of hot solutions, 316, 567; removing colouring matter, 208.

*Draining and Drying Crystals.*—Porous plate, 16; Buchner funnel, etc., 333; heat, 16, 33, 578.

*Fractional Crystallisation.*—Cooling, 33, 59, 141; differential solubility, 54, 121, 179, 178.

*Distillation*.—Fractional, 59, 141, 325, 482; with steam, 341, 383, 494.  
*Sublimation*.—Dry, 346, 494, 505, 602; with dry steam, 459.  
*Precipitation*.—On formation, 156; by diluting solvent, 381; by salting out, 341, 479, 515; by conversion into less soluble compound, 239, 245.  
*Extraction with Solvent*.—Dilute acids (basic compounds), 381, 538; alkalies (acids, phenols), 345, 543; ether (general), 331, 400, 401.

## CRITERIA OF PURITY.

*Boiling-Point*.—Moderate quantities, 4, 561; small quantities, 570.  
*Melting-Point*.—Moderate quantities, 33; small quantities, 55, 572.  
*Specific Gravity*.—Bottle method, 562 (or Westphal balance).

## OXIDATION.

*Air or Oxygen*.—Paraffins (aldehydes),\* 81; alcohols (aldehydes, acids), 47, 103.

*Alkali Fusion* (usually hydrolytic).—Fatty alcohols (acids), 56; cellulose (oxalic acid), 153; olefinic compounds (lower saturated compounds), 171; phenols (polyphenols), 401; indigo (indoxyl, etc.), 449, 322; alkaloids (proximate constituents), 544, 545.

*Chromic Acid Mixture*.—Primary alcohols (aldehydes), 98; secondary alcohols (ketones, acids), 111, 114, 115; tertiary alcohols (lower ketones, acids), 120; olefines (acids), 129; aryl-hydroxylamines (nitrosobenzenes), 341; aromatic amines (quinones), 399, 501; protected phenols (phenolic acids), 417.

*Chromic Anhydride (in Acetic Acid)*.—Naphthalene, anthracenes (quinones), 501, 503.

*Destructive*.—Combustion, 10; copper oxide, 10, 17; nitric acid, 20; sulphuric acid, 60.

*Halogen and Alkali (Hypochlorites, etc.)*.—Methyl ketones (acids), 109, 469; amides (lower amines), 274, 352, 535.

*Nitric Acid, Dilute*.—Complex alcohols (acids), 151, 152, 153, 163, 233; alkylbenzenes,  $\omega$ -halides (acids), 359, 361, 363, 444; dialkylbenzenes (substituted benzoic acids), 425.

*Nitric Acid, Concentrated or Fuming*.—Chloral (trichloroacetic acid), 142; complex ureides (simple ureides), 251; naphthalene tetrachloride (phthalic acid), 427; anthracene (anthraquinone), 503.

*Permanganate, Acid*.—Alcohols (acids), 32; aldehydes (acids), 100; ketones (lower acids), 109; oxalic acid (destructive), 155.

*Permanganate, Alkaline*.—Acetic acid (oxalic acid), 153; xylenes, xylene halides (phthalic acids), 427; olefines—cold, dilute (glycols), 129, 168.

*Silver Oxide*.—Aldehydes (acids), 100, 169.

*Sulphuric Acid*.—Naphthalene (with mercuric sulphate, phthalic acid), 427; piperidine (pyridine), 522.

## REDUCTION.

*Aluminium Amalgam*.—Haloid paraffins (hydrocarbons), 83; ketonic esters (hydroxy-esters), 207; nitrophenols (aminophenols), 384.

\*The substances in parenthesis are the resulting products.

## Summary of Operations and Agents 617

*Ferrous Hydroxide*.—Nitro-aldehydes (amino-aldehydes), 357.

*Formic Acid*.—Acids (barium salts: aldehydes), 99, 355; glycerol (allyl alcohol), 167.

*Hydriodic Acid (or Iodine) and Phosphorus*.—Middle and higher fatty acids (hydrocarbons), 93; complex alcohols (hydrocarbons), 160; complex acids (hydrocarbons), 193; hydroxy-acids, lactones (saturated acids), 175, 208, 234.

*Hydrogen*.—With reduced nickel: olefines (paraffins), 129; benzenoid compounds (cycloparaffinoid compounds), 370, 372. With platinum black: acetylene (ethane), 136.

*Iron and Acid*.—Nitro-compounds (amines), 322, 387, 497.

*Sodium and Alcohol*.—Nitriles (amines), 64, 362, 376; cycloid amines (alicyclic amines), 498, 522, 524; benzenoid acids—in amyl alcohol (alicyclic acids), 376; naphthols (alicyclic alcohols), 498.

*Sodium Amalgam*.—Aldehydes (alcohols), 100, 144; ketones (secondary alcohols), 111, 114; acid chlorides (aldehydes, alcohols), 39, 99; acids (aldehydes, alcohols, in special cases only), 56, 152; lactones (aldehydes, acids), 196, 233; phenols (alicyclic alcohols, ketones), 398; phthalic acids (hydrophthalic acids), 430.

*Stannous Chloride (or Tin) and Hydrochloric Acid*.—Nitro-compounds (amino-compounds), 322, 362, 419; diazonium compounds (hydrazines), 338; azo-compounds (constituent amino-compounds), 514, 516.

*Stannous Chloride, Alkaline (Stannite)*.—Diazonium compounds (elimination of group), 337.

*Zinc (or Copper-Zinc) and Water (or Acid)*.—Alkyl halides (hydrocarbons), 83, 232; nitriles (amines), 63; high fatty acids (alcohols), 56; aromatic nitro-compounds (nitroso-compounds), 341.

*Sulphides*.—Nitro-compounds (amino-compounds), 322; polynitro-compounds (nitroamino-compounds), 381.

*Sulphurous Acid and Sulphites*.—Quinones (phenols), 399, 501; diazonium compounds (hydrazines), 338.

### ETHERIFICATION.

*Esters by Direct Interaction*.—Acid and alcohol alone, 45, 155, 162, 299; with catalyst, 41; selective, 225; nascent acids, from salts, 42, 299.

*Esters from Limited Quantities*.—Alcohol limited (acid chloride, acid anhydride), 43, 208, 348; acid limited (silver salt, alkyl iodide), 34, 43.

*Acetylation and Benzoylation of Alcoholic and Phenolic Compounds*.—Acetyl chloride (cold), 208, (586); acetic anhydride, with sodium acetate or zinc chloride (hot), 232, (589); benzoyl chloride and soda (cold), 348.

*Ethers*.—Ordinary etherification (pseudo-dehydration), 27, 51; alkyl iodides, sodium alkyl oxides (in alcohol), 29, 51; iodides, sodium phenoxides (in water or alcohol), 329; chloroform, substituted chloroforms (ortho-esters), 87; aldehydes (acetals), 101.

### HYDROLYSIS AND HYDRATION.

*Water*.—Sodium alkyl oxides (alcohols), 17; alkyl sulphates (alcohols), 27; acid chlorides and anhydrides (acids), 37, 39; esters (alcohols), 43; chloro-acids (hydroxy-acids), 149; alkyl halides (aromatic alcohols), 361.



*Alkali Carbonates.*—Alkylene halides (glycols), 150.

*Caustic Alkalies, Aqueous.*—Alkyl halides (alcohols), 22, through esters, 112; esters (alcohol and acid), 42; fats (soaps), 53; amides (acids), 61; nitriles (acids), 63; chloral, chloracids, etc. (chloroparaffins), 142, 144; propiolic aldehyde (acetylene), 172; phloroglucinol (aliphatic compounds), 402; volatile substances, 22, 24, 87.

*Caustic Alkalies, Alcoholic.*—Fats (soaps), 50, 53.

*Alkali Fusion.*—Sulphonic acids (phenols), 330, 397, 398; influence of alkali, 401; of temperature, 398. (See also Oxidation.)

*Metallic Oxides and Water.*—Lead oxide: alkyl halides (alcohols), 112. Silver oxide: bromo-acids (hydroxy-acids), 206, 210; ammonium iodides (hydroxides), 277.

*Acids, Dilute.*—Ethers (at high temperature, alcohols), 29; amides (acids), 62; complex carbohydrates (simpler carbohydrates), 218, 220, 228; proteins (amino-acids), 288.

*Acids, Concentrated.*—Hydrochloric acid: nitro-paraffinoid compounds (acids, hydroxylamine), 301, 362. Hydriodic acid: methoxy-compounds (phenols), 329, 540. Sulphuric acid: ethers (alkyl sulphates), 29;  $\alpha$ -hydroxy-acids (aldehydes), 176; aromatic sulphonic acids (hydrocarbons), 320, (496); aromatic nitriles (amides, acids), 346, 498.

*Nitrous Acid (Pseudohydrolysis).*—Amides (acids), 62; primary amines (alcohols and phenols), 65, 274, 330; amino-acids (hydroxy-acids), 283. But see also Condensation, 284, 333.

*Hydration.*—Water or acids: unsaturated compounds, 144, 157, 442, 496.

#### HALOGEN SUBSTITUTION.

*Direct Chlorination and Bromination.*—Saturated and quasi-saturated compounds (halogen replaces hydrogen): paraffins, 83, 93, 94; fatty acids, 141, 142; saturated dicarboxylic acids, 206; benzene, 314, 315; aromatic acids, 352; toluene, 360, 415. Carriers and their mechanism: 141, 142, 315. Conditions of halogenating benzenoid compounds: 317, 326, 360, 415.

*Halogenation in presence of Water or Alkali (Hypochlorites, etc.).*—Aromatic compounds: Amines, phenols (halogen in nucleus), 325, (326), 330, 397; anilides (chloramines formed initially), 326. Aliphatic ketones, etc.: alcohols, methyl ketones (chloroform, etc., by incidental hydrolysis), 84, 109, 441, 469.

*Indirect Halogenation of Aromatic Compounds.*—Through amino-compounds, by diazonium interactions, 336, 337.

*Halogenation of Sensitive Compounds.*—Aldehydes (chloraldehydes), 143, 144; aromatic amines (chloranilides, chloranilines, etc.), 326, 421; azo-compounds, 517.

*Replacement of Hydroxyl or Oxygen by Halogen (Phosphorus and Sulphur Halides).*—Simple alcohols (alkyl chlorides, etc.), 19, 46; simple aliphatic and aromatic acids (acid chlorides, etc.), 37, 38, 319, 347; hydroxy-acids (chloracid chlorides, etc.), 175; phenols (halogen benzenes), 329; aldehydes (alkylidene chlorides, etc.), 101, 356; ketones (dichloroparaffins, etc.), 109; complex alcohols (chlorhydrins, secondary iodides, etc.), 112, 161, 168, 232.

## NITRATION.

*Dilute Nitric Acid*.—Higher paraffins (nitroparaffins), 300; alkyl-benzenes (aryl-nitromethanes), 362; cycloparaffins (alicyclic nitro-compounds), 371; phenols (mononitrophenols), 383.

*Concentrated Nitric Acid (or Fuming Acid)*.—Protected anilines (nitroacetanilides, nitranilines), 381, 421; mechanism, 382; nitrophenols (dinitrophenols), 386.

*Nitrosulphuric Acid*.—Iso-paraffins (nitro-isoparaffins), 300; benzenoid hydrocarbons (mono- or dinitro-compounds), 317, 380, 381; phenols (polynitrophenols), 385, 386.

*Indirect Nitration (Silver Nitrite)*.—Alkyl iodides (nitro-paraffins), 300; alkyl halides ( $\omega$ -nitro-compounds), 362.

*Esterification*.—Simple alcohols (with urea; alkyl nitrates), 299; complex alcohols (nitroglycerine, etc.), 162, 230.

## AMINO-SUBSTITUTION.

*Direct Action of Ammonia*.—Acid chlorides or esters (amides), 59, 62, 156, 349, 356; alkyl or alkyl halides (amines), 273, 275, 279, 362; aliphatic chloro-acids (amino-acids), 282, 286.

*Indirect Substitution*.—Nitro-compounds, etc., reduction (primary amines), 273, 301, 322, 362, 371; amides, oxidation (lower primary amines), 274, 535; nitriles, reduction (primary amines), 63, 362, 576; nitroso-compounds, reduction (primary amines and hydrazines), 339, 387.

*Protection of Amino-group from Further Action*.—Aromatic amines, acetylation (substitution and oxidation products), 325, 326, 381, 419, 420, 421; amino-acids, benzoylation (for resolution into active acids), 286, 348.

## SULPHONATION.

*Concentrated Sulphuric Acid*.—Benzenoid hydrocarbons (monosulphonic acids), 318, 416, 496; influence of temperature, 416; aromatic amines (e.g. sulphanilic acid), 326; mechanism (sulphonamic acids), 326; protected aromatic amines (e.g. toluidine-sulphonic acids), 421; pyridine (monosulphonic acid), 528.

*Fuming Sulphuric Acid or Chlorosulphonic Acid*.—Benzenoid hydrocarbons (monosulphonic acids cold; disulphonic or trisulphonic acids, hot), 318, 397.

## ADDITIVE ACTIONS.

*Alkyl iodides*.—Tertiary amines (methiodides, etc.), 277, 324, 521.

*Ammonia (Dry)*.—Aliphatic aldehydes (aldehyde-ammonias), 102.

*Bromine and Chlorine*.—Olefinic compounds (dibromides, etc.), 129, 169, 377; acetylenic compounds (tetrabromides, etc.), 137, 138; benzenoid compounds (hexachlorides, tetrachlorides), 317, 495.

*Halogen Acids*.—Olefinic compounds (hydrochlorides, etc.), 129, 171.

*Hydrogen and Oxygen*.—See Reduction and Oxidation.

*Hydrocyanic acid (Cyanogen Ions)*.—Aldehydes (cyanhydrins, hydroxy-nitriles), 102, 176, 364; ketonic compounds (cyanhydrins), 108, 235.

**Sodium Bisulphite (Concentrated Aqueous).**—Aliphatic methyl ketones (e.g. acetone sodium bisulphite), 108; complex aldehydes (e.g. glyoxal sodium bisulphite), 133; aromatic aldehydes (e.g. benzaldehyde sodium sulphite), 356.

**Sulphuric Acid.**—Unsaturated hydrocarbons (sulphates, alcohols, etc.), 129, 137.

#### DIRECT DECOMPOSITIONS.

**Resolution by Distillation.**—Polycarboxylic acids (simpler acids), 165, 191, 192, 204, 215, 433; phenolic acids (phenols), 408, 411; amino-acids (amines), 283, 352.

**Resolution by Heating with Alkali.**—Carboxylic acids (hydrocarbons, etc), 82, 345, 427, 521, 529; substituted carboxylic acids (substituted hydrocarbons, etc.), 283, 408.

#### DEHYDRATION, DEHALOGENATION AND CONDENSATION.

**Dehydration.**—By acetic anhydride: aldoximes (nitriles), 103, 476; aldols (unsaturated aldehydes), 441. By heat: ammonium salts (amides), 62; ortho-dibasic acids (anhydrides), 195, 199, 201, 427; hydroxy-acids (lactones or unsaturated acids), 170, 177, 196, 201. By potassium bisulphate: glycerol (acrolein), 168; terpineol (limonene), 464. By phosphorus pentoxide: amides (nitriles), 63, 156. By sulphuric acid (pseudo-dehydration): alcohols (olefines, ethers), 27, 128.

**Dehalogenation.**—By aqueous alkali: alkyl iodides (olefines), 112. By alcoholic alkali: alkyl polyhalides (unsaturated compounds), 128, 133, 135, 171, 377, 445, 446. By soda-lime: alkyl and alkylene halides (olefines, acetylene), 128, 133. By zinc-dust: alkyl polyhalides (e.g., ethylene bromide, iodoform, to ethylene, acetylene), 128, 135.

**Condensation and Polymerisation of Aldehydes and Ketones.**—By acids: aldehydes (complex cyclic ethers), 102, 104; acetone (unsaturated ketones), 109, 133; aromatic and aliphatic aldehydes (unsaturated aldehydes), 443. By alkalis: formaldehyde and lower aldoses (hexoses), 240; aldehydes (aldols), 189. By alkaline cyanide: aromatic aldehydes (benzoins), 475. By alkalis, with subsequent hydrolysis (possibly): Formaldehyde and aromatic aldehydes (alcohol and acid), 104, 361.

**Condensation of Aldehydes, Ketones and Esters.**—By sodium ethoxide (Claisen condensation): acetone, esters (e.g. oxalacetate, acetylacetone), 188; benzaldehyde, ketones (benzylidene-compounds), 357, 454, 536; ethyl oxalate, ethyl dimethylglutarate (cycloid keto-ester), 458. By acetic anhydride (Perkin condensation): aromatic aldehydes, acetic acids (unsaturated acids), 441. **Esters alone.**—Ethyl acetate (acetoacetate), 183, 185; ethyl malonate (phloroglucinol-dicarboxylate), 402; ethyl succinate (tetrahydroquinone-dicarboxylate), 403.

**Nitrogen Condensations.**—**Phenylhydrazine:** aldehydes, ketones, acids (aldehyde-hydrazone, ketone-hydrazone, acid hydrazides, osazones), 103, 109, 176, 233, 238, 239. **Hydroxylamine:** aldehydes, ketones (aldoximes, ketoximes), 103, 109, 476. **Semicarbaside:** aldehydes, ketones (semicarbazones), 296, 356. **Aniline:** aromatic aldehydes (aldehyde-anilines), 356. **Nitrous acid:** methyl or methylene-ketones (isonitroso-

compounds, aldioximes), 303, 454, 536; amino-esters, aromatic amino-compounds (diazo-esters, diazonium compounds), 333, 336; secondary amines, tertiary aromatic amines (nitroso-compounds), 276, 324, 387. *Ammonia*: aromatic aldehydes (hydramides), 356. *Chloroform*: amines (alcoholic alkali; isocyanides), 85, 331.

*Other Condensations*.—Carbon dioxide, chloroform (Kolbe's and Reimer's reactions): phenates (aromatic hydroxy-acids, aldehydes), 406, 407, 409. Glycerol (Skraup's reaction): aniline (quinolines), 520, 531. Formic acid: sodium-formate (oxalate), 127.

#### SYNTHETIC METHODS.

*Direct Synthesis*.—Methane (with formaldehyde, 81, methyl alcohol 104, and carbohydrates, 104); from carbon (element, monoxide, disulphide, aluminium carbide), 82, 83. Acetylene (with ethylene and alcohol, 136, 129, hydrogen cyanide, 137, benzene, 314, pyridine, 521); from calcium carbide, 135. Formic acid; from carbon monoxide and dioxide, 49. Acetic acid (with acetone, 107); from carbon disulphide, 142. Oxalic acid; from carbon dioxide, 135. Thiocyanates (with hydrogen cyanide, 258, and urea, 247); from carbon disulphide, 270. Urea; from carbon monoxide and dioxide, 246.

*Cyanide Synthesis*.—Formic acid and methyl alcohol; from hydrogen cyanide, 70. Acetic acid and ethyl alcohol (with acetaldehyde, 100, 98, and ethyl acetate, 47); from methyl alcohol, 71, 72. Isobutyric acid, from acetone, 119. Malonic acid (with numerous synthetic products, below); from acetic acid, 191. Succinic acid (with malic and tartaric acids, 206, 210); from ethylene, 194. Benzoic acid (with benzaldehyde, 355); from benzene, 346.

*Cyanhydrin Synthesis*.—Lactic acids; from aldehyde, 176. Tartaric acids (through glyoxal, 152); from alcohol, 211. Citric acid (through glycerol, 161); from acetone, 215. Glycine; from formaldehyde, 282.

*Acetoacetic Synthesis*.—Alkylacetic and dialkylacetic acids, 187, 188; alkylacetones and dialkylacetones, 187, 188; malonic acid, 191; uric acid, 252; collidine, 527; antipyrine, 554; pyrones, 556; from ethyl acetate, through ethyl acetoacetate, 183.

*Malonic (and Cyanacetic) Synthesis*.—Alkylacetic and dialkylacetic acids, 192, 193; purine compounds, 255; cycloparaffinoid compounds, 375, 376; phloroglucinol derivatives, 402; terpenes, 466; proline, 552; from acetic acid, through chloracetic and cyanacetic acids, 141, 191.

*Cinnamic Synthesis*.—Cinnamic acid and aldehyde, 441, 443 (with coumarin, 443, tyrosine, 446, indigo, 446, quinoline, 574), from benzaldehyde and acetic acid.

*Various Syntheses with Halogen Compounds*.—Magnesium alkyliodides: secondary alcohols (from aldehydes), 112, 122; tertiary alcohols (from ketones and esters), 120; carboxylic acids (from carbon dioxide), 346 (572). Zinc alkyls: ketones (from acid chlorides), 110. Sodium condensations: paraffins and cycloparaffins (from alkyl halides), 92, 232, 373; alkyl-benzenes (from alkyl and aryl halides), 359. Aluminium chloride condensations: aromatic ketones (hydrocarbons, acid chlorides), 350; alkyl-benzenes (hydrocarbons, alkyl chlorides), 360, 482; rosaniline dyes (through alkyl-benzenes), 483.

*Pseudo-Natural Syntheses*.—Carbohydrates, 104, 240, 224; fats, 162; polypeptides, 291; terpenes, 465; pyridine alkaloids, 529, 552.

## QUALITATIVE ANALYSIS

The following scheme will be found useful in determining the nature of artificial mixtures of the organic compounds specified below with inorganic acids, bases, etc. (The tests for the individual compounds are given under the respective compounds.)

### LIST OF SUBSTANCES

I. ACIDS.—(*Precipitable by calcium chloride; precipitable or coloured by ferric chloride; precipitable by mineral acids*):—

- i. Calcium salts precipitable: oxalates (§ 122), white, immediate.; tartrates (§ 159), white, on rubbing; eltrates (§ 164), white, on boiling with ammonia.
- ii. Ferric salts coloured, and precipitable in cold: benzoates (§ 268), buff, pulverulent; hippurates (§ 271), brown, flocculent; succinates (§ 150), red, gelatinous. [Tartrates also precipitated from very concentrated solutions, and cyanides from slightly alkaline solutions.]
- iii. Ferric salts coloured and precipitable on boiling: acetates (§ 29), red solution, brown precipitate; formates (§ 44), same.
- iv. Ferric salts coloured and imperfectly precipitable: gallates (§ 311), black; tannates (§ 311), black; ferrocyanides (§ 202), dark blue.
- v. Ferric salts or compounds coloured and soluble; thiocyanates (§ 210), red; ferriocyanides (§ 202), greenish-brown; salicylates (§ 308), violet; phenates (§ 254), violet.
- vi. Convertible into compound precipitable by ferric chloride: Simple cyanides (§ 201).
- vii. Insoluble in acids: uric acid (§ 195); benzoic and succinic acids; phenol (oil from concentrated solution).

II. ALKALOIDS AND AMINES.—(*Precipitable by sodium carbonate or caustic soda*):—

- i. Solid precipitate: strychnine (§ 402); quinine (§ 399); morphine (§ 402).
- ii. Oil (from concentrated solution): aniline (§ 249).

III. AMIDE.—Soluble in water; hydrolysable by concentrated caustic soda; urea.

IV. CARBOHYDRATES.—(*Precipitable only by special agents; non-volatile*):—

1. Soluble in cold water: cane-sugar (§ 167), readily; milk-sugar (§ 170), with difficulty; glucose (§ 168), readily.
- ii. Soluble only in hot water: starch (§ 176).

**V. ALCOHOLS AND DERIVATIVES.**—(Distillable alone, or with alkalis or acids; and precipitable only by special agents):—

- i. *Stable to alkalis*: alcohol (§ 19), *readily volatile*; glycerol (§ 127), *difficultly volatile*; [acetic and formic acids].
- ii. *Decomposed by alkalis*: chloral (§ 113), *immediately*; chloroform (§ 73), *with concentrated alcoholic alkali*; [hydrocyanic acid].

### PROCEDURE

#### A. PRELIMINARY EXAMINATION OF A SOLUTION.—

- i. Note colour,<sup>1</sup> odour<sup>2</sup> (especially on warming); reaction to litmus.
- ii. Evaporate some to dryness on water bath, and note whether no residue,<sup>3</sup> syrupy residue,<sup>4</sup> or solid residue. Examine solid residue by B.
- iii. Distil some from test tube with cork and bent tube leading to bottom of second test tube cooled in beaker of water; note odour and reaction of distillate, and test by A-i and C, and specially.<sup>5</sup>
- iv. If solution acid, distil with slight excess of caustic soda, and examine distillate by A-i and C.
- v. If solution alkaline, distil with slight excess of dilute sulphuric and examine distillate by A-i and C.

#### B. PRELIMINARY EXAMINATION OF SOLID.

- i. Heat a little in bulb-tube and note odour,<sup>6</sup> melting,<sup>7</sup> partial or complete volatilisation,<sup>8</sup> blackening.<sup>9</sup>
- ii. If residue remains in bulb-tube, heat on fragment of porcelain and examine carbon-free residue (if any) for metals.<sup>10</sup>
- iii. Boil substance with water. If entirely soluble, proceed to A-i-iii-iv and C; if partially soluble (evaporate few drops, filtered, on watch-glass at 100°), filter and boil residue with small quantities of water as long as anything is dissolved. Examine solution by A-i-iii-iv and C.
- iv. Heat solid, or insoluble and soluble portions separately, to redness on fragment of porcelain. If metallic residue, boil *portion* with sodium carbonate, and filter (see C-i), and examine solution by A-i-iii-iv and C. Precipitate may contain alkaloids; shake with a little cold water and ether-chloroform, latter dissolves alkaloids.

<sup>1</sup> Iron and copper salts coloured; organic solutions often turn brown from oxidation.

<sup>2</sup> The following have characteristic odours:—Alcohol, chloral, chloroform, aniline, phenol, tannin; acetic, formic, hydrocyanic and benzoic acids, and certain of their salts.

<sup>3</sup> The following are completely volatile at 100°:—Free acetic, formic and hydrocyanic acids; water, alcohol, chloral, and chloroform.

<sup>4</sup> The following are syrupy:—Glycerol; free phenol; sugars (milk sugar may crystallise quickly); free tartaric and citric acids (crystallise only slowly).

<sup>5</sup> The following are easily volatilised:—Alcohol, chloral, chloroform, and free acetic, formic and hydrocyanic acids; the following with difficulty: glycerol, free benzoic and succinic acids; aniline (from alkaline solution), phenol (from acid solution).

<sup>6</sup> Burnt leather odour=uric acid, alkaloids (nitrogen); burnt sugar=sugars, tartrates; aromatic=benzenoid acids; suffocating=succinates, citrates.

<sup>7</sup> Sugars, urea, and many acids and salts melt easily.

<sup>8</sup> Completely or partially volatile, see Notes 3 and 5.

<sup>9</sup> Blackening=carbohydrates, tartrates, etc.

<sup>10</sup> Solid residue on ignition contains all metals except mercury and arsenic, and possibly antimony; examine for these specially.

- v. If no residue on ignition, and solid insoluble,<sup>11</sup> dissolve in dilute sulphuric acid or caustic soda.

C. EXAMINATION OF SOLUTION.

- i. If acid, neutralise; add solid sodium carbonate, a little at a time, as long as there is violent effervescence, then add more of the acid solution until the whole is distinctly acid; then neutralise with ammonia. Precipitate contains metals (except antimony and, perhaps, lead; and iron and copper in presence of hydroxy-compounds); these must be eliminated with sulphuretted hydrogen (or ammonium sulphide); and alkaloids (B-iv).
- ii. If alkaline, neutralise with dilute hydrochloric acid, and note odour. If precipitate, see I-vii.
- iii. To portion of filtered, neutralised solution add ferric chloride; if precipitate, filter off, and examine for acids, I-ii-iv; boil filtrate, and if further precipitate, filter off and examine for acids, I-iii; if filtrate still coloured, examine for acids, I-iv-v.
- iv. To fresh portion add ammonium chloride, ammonia (slightly alkaline only) and plenty of calcium chloride (half volume); note whether precipitate immediately, or on rubbing, or only on boiling with ammonia (I-i). Ammonia may precipitate alkaloids (II-i, B-iv).
- v. Examine for alkaloids, first by general tests, and then, if present, by special tests; aniline always specially, after ether-chloroform extraction.
- vi. Examine for urea, sugars, and starch.
- vii. Examine for cyanides (beaker tests); mercuric cyanide must be decomposed with metallic zinc.
- viii. Examine for uric acid.

D. EXAMINATION OF MIXTURE.

If two organic substances are present, the second is found in the same way, bearing in mind that its reactions may be obscured or modified by the presence of the first. Volatile and non-volatile substances are readily separated by distillation; precipitable and non-precipitable by filtration.

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<sup>11</sup> Probably uric acid or free alkaloid.

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